WITHDRAWN

17249

HANDBOOK
of
TOXICOLOGY

Volume III: Insecticides

A Compendium

WITHDRAWN
DEPT. OF INSECTICIDES AND FUNGICIDES
ROTHAMSTED EXPERIMENTAL STATION
HARPENDEN, HERTS
ENGLAND

By

WILLIAM O. NEGHERBON

WITHDRAWN
ROTHAMSTED
EXP. STATION
27 JAN 1986
HARPENDEN

Prepared under the Direction of the Committee
on the Handbook of Biological Data

DIVISION OF BIOLOGY AND AGRICULTURE
THE NATIONAL ACADEMY OF SCIENCES
THE NATIONAL RESEARCH COUNCIL

WITHDRAWN
OGG (WEST) BUILDING
LIBRARY

W. B. SAUNDERS COMPANY
Philadelphia and London

632.9/HA

The Library of Congress has cataloged this book as follows:

Handbook of toxicology. Prepared under the direction of the Committee on the Handbook of Biological Data, Division of Biology and Agriculture, the National Academy of Sciences, the National Research Council. Philadelphia, Saunders. 1956–59. 5v. 28 cm. Includes bibliographical references. Contents.—v. 1. Acute toxicities of solids, liquids and gases to laboratory animals, edited by W. S. Spector.—v. 2. Antibiotics, edited by W. S. Spector.—v. 3. Insecticides, by W. O. Negherbon.—v. 4. Tranquilizers, edited by R. M. Grebe. v. 5. Fungicides, edited by D. S. Dittmer. 1. Toxicology. I. National Research Council. Committee on the Handbook of Biological Data. RA1211.H32 (615.9) 56–6976 rev. 2.

© 1959, BY W. B. SAUNDERS COMPANY

COPYRIGHT UNDER THE INTERNATIONAL COPYRIGHT UNION

All rights reserved. This book is protected by copyright. No part of it may be reproduced in any manner without written permission from the publisher, except for any purpose of the United States Government.

Made in the United States of America

INTRODUCTION

In sponsoring the Handbook of Toxicology, the United States Air Force, through the Wright Air Development Center, foresaw from the outset a volume, or at least a section, on insecticides. The present book, dealing with the toxicity of insecticides and such ancillary substances as acaricides (miticides) insecticide synergists, repellents, etc., is the outcome. The goal of this book has been to bring together as completely as possible and in convenient form data—preferably quantitative, tabular, and comparative—derived from valid tests by explicit methods, on the subject of insecticide toxicity.

Implicit in the subject of insecticide toxicity is the topic of hazard to man, to domestic animals and plants, and to plants and animals in nature. Hazard may be particular, unique to certain circumstances or in absence of certain reasonably attainable precautions, or it may be universal and ever-attendant upon the simple existence of a toxic agent. Hazard may accompany the synthesis or manufacture, the compounding or formulation, or the general or special use of an insecticidal substance. During synthesis or manufacture, hazard may be far more acute than in final use, since the primary materials or processes may be far more toxic than the end product, or be far more difficult to control in their harmful potential. The inverse, of course, may just as easily be the case. Hazard and toxicity, then, must be carefully differentiated but the degree of hazard cannot fully be measured without exact knowledge of the toxicity. Hazard and risk, biologically speaking, are inherent in insecticides as in any other biologically potent agent.

By definition, an insecticide is a substance, a mixture of substances, or an agent used to kill and thus to control insects and related arthropods. In actual use, insecticides are intended to apply only to species harmful or annoying to man and his chattels or property. Unfortunately, in most cases the insecticide must be applied to the undesirable insect in a context of other living organisms, plant or animal, which may be also subject to the life-harming powers of the insecticide. The goal, plainly, is to have insecticides which are highly specific in their action, acutely effective in harmful properties for the undesirable forms of life, while being innocuous or only slightly, and so controllably, harmful to other living forms. With chemical agents as insecticides it is not always easy to attain such specificity. What may be lethally harmful to insects by in any way altering or disturbing their normal vital processes may entail harm for other living organisms. It is necessary, however, to guard against an automatic assumption that high hazard exists in the use of any and every insecticidal agent. Hydrogen cyanide is a gas acutely toxic for virtually all animal organisms, and nicotine is an alkaloid which, unit for unit, is almost incomparably poisonous for higher animals; yet both these substances have long been used for insect control in a completely routine manner, with proper precaution, by persons not chemists, pharmacologists, toxicologists or zoologists, and without harm to themselves. The important thing is to know and understand where and under what conditions even a highly poisonous substance may be employed with a minimum of hazard. For long-familiar insecticides the conditions of use, of precaution, and of control are, on the whole, well-known. But nowadays new insecticides are multiplying upon the scene in many guises, under many names, in many formulations. Until about twenty years ago, new insecticides made their appearance in a thin trickle. With the arrival of DDT, the trickle became a freshet, and the freshet now attains the dimensions of a flood. But advances in knowledge of the special nature of insects and their close relatives have also multiplied—many of these advances resulting from a search for methods of control and the test of putative or potential insecticides. By knowing more fully the special nature of insects and those weaknesses peculiar to them, advantage may be taken of such special attributes to attack the insect while leaving safe other living organisms.

By concentrating primarily on the toxic properties of insecticides, the present work might expect to achieve usefulness as a general guide to the degree of hazard, viewed broadly, that attends the use, under reasonably well-defined conditions, of any insecticide presently in general use or rapidly achieving general use. The comments made under Acknowledgments have already indicated that any value this book may have rests solidly on the original scientific data of a host of workers. Only by considering and comparing many data, and allowing for various methods used under specified conditions, is it possible to consider the range of action of a particular agency. This work considers data drawn from controlled laboratory experiment under defined conditions as well as data, and certain "value" conclusions, derived from field experiences whose conditions are far more difficult to define and control. A recognition both of the relatedness and the essential differences that distinguish the classes of data gathered by these two general methods has led to their being quite strictly set apart from each other in this book. Although this will help to provide understanding, forewarning, and control of hazards associated with insecticidal use of chemical agents, such putative utility must be a by-product—a consequence of knowledge presented disinterestedly and without bias. Comprehension of this ideal does honor to the United States Air Force which, in the immensity of its activities, has recognized the primacy of knowledge and sought to promote it in so many fields.

Aside from usefulness in the assessment and control of hazard, other useful results may arise from the comparative treatment of the data as these concern groups or families of substances related chemically and structurally, or related by an essential similarity in mode of detailed action. Toxic action is physiological action, biochemical action. The toxic action as such may be the one on which we focus attention, but that toxic action may shed valuable light on the general physiology of a biological group of such high importance and interest as the insects. Thus, as Sir Francis Bacon long ago insisted when induction as a method, if not as a practice, was young—data brought together in an orderly and comparative way may in the hands of the thoughtful and imaginative readily suggest fertile associations and fruitful generalizations.

A given insecticide is not equally effective or similar in its action upon all insects. This very fact may lead to deeper knowledge about both the insects and the nature of the insecticide. The quest for new, useful agents of chemical control of insects is nowadays far from being wholly and blindly empirical, as once it was. Newer knowledge of insect physiology—and what may rightly be termed insect pharmacology and pharmacodynamics—has revealed that certain general types of chemical structure act on insects. Such information makes possible a more clearly-directed search for agents with sharper and more specific insecticidal use. Indeed, it may be said that to a fair extent insecticides may now, in a chemical sense, be designed deliberately. In that activity this book may, in a very practical manner, be helpful.

From the outset it was deemed more fruitful to deal generally with the toxicity of insecticides for all living organisms, whether mammals or other vertebrates, insects, other invertebrates, or plants. Also it was apparent that a work on insecticide toxicity would be gravely incomplete and grossly limited if it ignored a proper setting forth of what is known or reasonably conjectured about the modes of pharmacodynamic action (and so toxic action) of the compounds dealt with. This imposed another dimension on the work and required an orderly comparative treatment of physiological, biochemical, pharmacological and pharmacodynamic data, as well as of the pertinent aspects of the physical and chemical properties of the compounds.

Emphasis, or apparent emphasis, upon the toxicity of insecticides entails certain touchy consequences. The risks and hazards of insecticide use have been both grossly exaggerated and grossly underestimated and they will continue to be until sufficient data are properly available to give unbiased persons a basis for valid judgment. One extreme view finds an inherent harmfulness in the use of any chemical agent in agriculture or forestry and holds that a healthy plant (brought, of course, to maximum vigor by the use of organic fertilizers only!) tolerates and overcomes any and all insect attack—a view often coupled with the conviction that insecticides are an unmitigated threat to the balance of nature. Another extreme view results in an indiscriminate, overenthusiastic use of insecticides without regard for real problems of toxic hazard in their many aspects. Attainment of some golden mean is the hope and the object of this book. Certain dangers to the balance of nature may always be a possible consequence of large-scale human activities. Yet, it may be reasonably expected that man, having an ingenuity sufficient to upset the balance of anything so majestic as nature, will find in himself an ingenuity equal to redressing the balance. It is quite true, for instance, that large-scale, intense use of certain chlorinated hydrocarbon insecticides to control leaf-eating insects may bring on great upsurges in the numbers of sucking arthropods, such as aphids and mites, because of a coincident decimation of their natural enemies. Such a situation calls for more knowledgeable use of combinations of agents having a range of action sufficient for the simultaneous control of the several harmful forms. A deeper understanding of the subtleties of the natural balance is needed and a greater foresight in testing and evaluating putative insecticides under many circumstances.

Such dangers do not diminish the value of insecticides wisely and skillfully used. Even the achievement of complete specificity in insecticides would not entirely remove all hazards, and certainly not the hazard to the balance of nature. Even those insect species supremely noxious to man have their place in that balance. The imperative laid upon man is that of judgment founded on wide knowledge in weighing one danger, one hazard, against others and mastering them all. The balance of nature on the North American continent was no doubt in quite suitable adjustment before the arrival of the Japanese beetle. A specific, or a method, that would once and for all remove this undesirable immigrant from the North American scene would not, wisely applied, harm nature by one bit.

This book has its severe limitations—limitations self-imposed in the original conception of the work. Some of these are later described so as to indicate to what extent the work proposes to have valid scope and wherein it does not propose to have competence.

Thorny problems attended the conception and the growth of the work. It was imperative to present the facts in such a way that the source of any particular one might be quickly apparent to the reader, and to accomplish this without loading the text with an excessive freight either of direct bibliographical citation or of numbers referring to a cumulative bibliography. The bibliographic problem was a major one because of wide variations of data referring to the same or similar situations. Large variations in results offered by several workers do not imply that all are wrong or that one alone is right. Method of test and experiment, nuances which attend a given occasion, the nature of the test insects or animals themselves—a multitude of factors too numerous to pursue—are at play as sources of variation. These the reader must be able to trace and evaluate from the sources. In this field as in others, the best and most useful methods have not yet necessarily come to light or moved to the fore. At this stage it appears that data attained by many methods properly and honestly applied must be presented. Indeed, the variety in the data itself points to the inherent complexity of problems and to the need for deeper knowledge and new approaches.

How to set forth information so various and from so many sources was answered (wisely, it is hoped) by combining, as the nature of the data demands, tabular, semi-tabular and frankly textual (but outline) methods. Running text was the resort in fields and topics which resist tabulation or where tabulation might mislead by producing a false impression of finality and certitude. This last is a risk ever-present in tabulating and presenting together data from many disparate sources without adding details or indications about method or the conditions of experiment or observation. As opposed to tabulations with an elaborate and confusing apparatus of footnotes, a simple outline text was deemed more useful for much material. By setting text statements in outline with designation by numbers and letters, attribution of facts to a marginally indicated source became possible.

The task undertaken loomed appallingly great when it was soon evident that data contributed *ad hoc* by their originators would not be forthcoming with sufficient completeness and balanced emphasis or, above all, within a practical period of time. To bring off the project at all, the author had to gather the data directly and all but wholly from published sources. The gathering of materials, their organization, and the composition of the manuscript took from September 1955 to March 1957. Contemporaneous data were added steadily during the months of preparation. Pertinent additions were made to the text as completed in March 1957 from publications appearing through the whole of 1957. Addition of such supplemental recent data ended in February 1958. These facts are recorded to allow the reader to judge the contemporaneity of the book's content.

A word of caution is needed. The Table of Contents shows many names of substances quite widely familiar as designations for insecticides in the open market or frequently appearing among the active ingredients listed for insecticides sold under various proprietary names. At almost any point a glance at the text will show various insecticidal substances comparatively treated in the tables in terms of toxicity. Comparative rankings founded on degree of toxicity measured in various ways under controlled experimental conditions have, to be sure, their proper worth in evaluating insecticidal potential. They have, however, little to do with the relative merit of this product or that as ingredients of field, garden, or household insecticides under conditions of diverse general use. Such ranking must not in any way be taken to mean that this book, the author, the sponsors, or the publishers individually or collectively recommend one substance over another or one insecticide in preference to another in any situation. Not even in those instances where it may appear that in field experiences substance "A", for example, was ineffective or proved less effective than substance "B" in degree of mortality yielded or extent of control given for a particular insect species does this imply a general value judgment of the relative worth of substances "A" and "B" under wide and diverse conditions of use. In the laboratory a compound may show great range of useful activity against the relatively small number of test insects usually employed as laboratory subjects. If it is as an insecticide of wide "spectrum" that the compound is intended it may well be far less promising against the multitude of species of undesirable insects to be coped with in nature. A compound which in a specific kind of laboratory test proves to be the most toxic of a group or series of compounds may under field conditions (or even in another type of controlled test) be precisely the least effective because of other physical or chemical properties.

As an example, nicotine sulfate under some conditions and acting upon certain insect species is a superb and even ideal contact insecticide. Unit for unit, nicotine sulfate may be, judged in tests based on LD_{50} or other criteria, greatly more toxic than a substance designated as "X" when both are tested by intraparenteral injection into individuals of a particular insect species. Let us assume, however, that "X" is designed for use as a residual insecticide of long-lasting action—a role in which it has proved valuable. For all its effectiveness as a contact insecticide nicotine sulfate as a residual insecticide is all but useless because of its notable evanescence. Under specific conditions the high contact toxicity combined with evanescence may be just the combination of properties most to be desired. Under other conditions the property of evanescence may entirely cancel the advantage of high toxicity. Toxicity *per se* is but one of the attributes called for in an effective insecticide and need not be, categorically, the most determinant of effectiveness. Actually, under some conditions, extreme toxicity may prove a stumbling block to practical use of a substance as either a general or specific insecticide. All this is by way of saying that the data brought together in this book are expected to have value when judiciously and properly interpreted or used in the context for which they were originally, and in the present publication continue to be, intended.

It is not proposed as part of the scope of this book, to give an orderly treatment, however abbreviated, of the history of insecticides or of man's essays to fend off the depredations of insects. It may not be amiss, nevertheless, to remark here that man from the start suffered in his body and in his goods the damage and loss pressed on him by a host of insect species. Man's attainment to the rank of husbandman and cultivator certainly posed for him in a more acute form the endless contest between himself and these insidious and extraordinary adversaries. Just as surely he must very early have noted the beneficence and usefulness of many insects, notably the silkworm and the bee, and been excited by the vivid beauty of others. A testimony to the latter is the jewelry of irridescent beetle wing cases worn by the Papuans. Attempts to evade the despoliation of his crops, gardens, and animals by insects, doubtless led man from Neolithic times, if not earlier, to meet his competitors the insects by many means, some perhaps crudely chemical. In the folklore of peoples there is mention, and in the folkways there is use on a local scale, of plants and plant products which have or are reputed to have insecticidal worth. One need only recall that some peoples accounted primitive have shown high skill and cleverness in the use of plant products as fishing and hunting poisons. The use of rotenone-bearing plants as fish poisons or stupefiants is a case in point. The fly-killing properties of some daisy-like flowers containing pyrethrins, where these are native, have evidently been noted from immemorial times. Homer has sung of the "divine and purifying powers" of sulfur burned in ritual purification.

With what success man fought his insect foes there is but little record until quite recent times. But, whatever man's success may have been on a small scale in earlier, or on a more far-reaching scale in later times, there is to this day no triumph of conquest-by-extinction of a single noxious species. However, there have recently been great triumphs in chemical insect control on a regional scale, even to the point of elimination of some species from wide regions, but a permanent end to the struggle on any front is yet far to seek.

Weapons of great subtlety are being devised, some of them exceedingly ingenious. An interesting example is the use of high-energy, short-wave rays, (such as those from radioactive cobalt) to irradiate male warble flies to the point of extinction or suppression of normal spermatogenesis and the subsequent release of these treated males into the environment. Such males suffer no obvious disability other than the one mentioned nor are they at a disadvantage behaviorally in the external aspects of sexual competition. However, their insemination of, or copulation with, females—an act taking place but once in the life-cycle of the latter—leads to a life-long laying of sterile eggs. But the wheelhorses of insect control will probably continue to be chemical agents, increased in number, reduced in price, cunningly designed and refined for ever enhanced and more specific action. Occasions may well arise on which we may, after a period of desuetude, resume the use of some of the older agents. Calcium and lead arsenates—insecticides of ancient lineage—were still sold ten years ago to the extent of fifty-five million (55,000,000) and ninety million (90,000,000) pounds respectively. Sulfur, for fungicidal and insecticidal purposes, was used in the amount of two hundred million (200,000,000) pounds. In the same year the modern insecticide DDT was used in the amount of forty million (40,000,000) pounds.

The use of arsenic compounds as insecticides is commended in written accounts dating to the last quarter of the 17th century and their practical and effective use certainly antedated that period. The fungicidal effects of copper compounds on diseases of the vine in European vineyards was recognized in late Renaissance times. The insecticidal and fungicidal powers of copper and arsenic found employment as Paris green in the last quarter of the 19th century. From such sources stemmed a considerable arsenal of mineral insecticides many of high usefulness to the present time. Recognition of the insecticidal value of some plants, notably derris, appears to have originated in China. The Romans appear to have used Veratrum insecticidally and rodenticidally. No one knows how or where the numerous species of plants showing insecticidal virtues may first have been used. Kerosene emulsions to control several sucking insect pests came into use in 1877. A quite respectable group of synthetic organic insecticides was in hand beginning early in the first third of the present century, among them several fumigant agents such as methyl bromide, carbon disulfide and para-dichloro benzene. Thiocyanates and thiocyanoacetates were added to the armamentarium shortly after, as well as the highly potent and effective nitrophenol family of compounds. And, as noted before, since the advent of DDT as an insecticide in Switzerland in 1939 the flood-gates have been opened and synthetic organics have come to dominate the scene.

In arriving at the insecticides presently in vogue thousands of compounds from the chemical stockroom have been tested as well as hundreds of others synthesized *ad hoc* or available as byproducts of other investigations. Seeking substances to control and repel insects and other arthropods of medical interest led to the systematic testing of some eleven thousand (11,000) compounds by the Orlando, Florida laboratories of the United States Department of Agriculture alone. And so the story and the search go on.

The extent of the need for chemical control of insects, and indeed, for any other kinds of practical or available control, may be measured by the fact that of some eighty thousand (80,000) species of insects in North America, ten thousand (10,000) are noxious species of more than casual consequence. Their depredations are vast, estimated for the United States alone to cost some two billions (2,000,000,000) of dollars and to entail a loss of some ten per cent (10%) of the country's agricultural crop.

The Table of Contents of this book will be found to list one hundred and eighty-eight (188) sections. Of these one hundred and sixty-four (164) concern individual, specific insecticidal substances or ancillary agents. Twenty four sections—some quite lengthy, others short—deal with general topics or treat collectively certain properties and aspects of well-defined families of related compounds which show broad similarities of chemical structure and mode of physiological and pharmacodynamical action. The reader will certainly ask how and why the comparative handful of 164 insecticides dealt with in this book was selected from the many compounds having some insecticidal virtues and from the great number of compounds systematically tested. The criterion has been that a substance, on the basis of tests, must be an effective insecticidal agent either in general use or in economically significant specific use, or must have so qualified in the immediate past or give evidence of being about to attain such usefulness.

Some general description of the form chosen for the presentation of the subject matter will provide guidance in the use of the book and an idea of its scope and its limitations and thus of its competence and validity. First, it will be seen that each compound or insecticide has been dealt with individually, as an entity, with all pertinent material relating to the compound gathered under the heading—which is the compound's name. Since many compounds are similar in many aspects of their chemistry and action, this has led to rather frequent repetitions and even to multiple appearance under several compounds of the same comparative tabulation, but only slightly rearranged in each case to bring to the top the name of the compound specifically the subject of that section. This has come about, and is believed justified, because it was considered that a handbook should present succinctly in one comprehensive section or chapter everything pertinent to one compound or insecticide—without the annoying necessity of multiple cross references and endless leafing of pages in widely different parts of the book. A certain amount of repetition was considered a small price to pay for having the data coherently grouped in each separate section. Where common properties and modes of action, etc., are so similar as to have led to voluminous repetition of much the same set of facts, a general section was added for that particular natural group of compounds. Cases in point are the extensive general treatments of Organic Phosphates, Dinitrophenols, Fumigants, etc., in addition to the specific treatments of the individual members of each of these groups.

For simplicity's sake, individual sections of the book (those dealing with particular specific compounds), as well as the general sections, are presented in alphabetical order. Compounds are listed by their most common names, this being true even if such designations are trade names or names made up *ad hoc*, when these have reached currency of use. In the absence of such current common names, strict chemical designations are used. Also, each section at the very beginning gives the more usual synonyms by which a substance may be designated.

In the index of chemical names, where all compounds mentioned in section headings or text are given, all available designations for any compound are set down alphabetically, with appropriate cross-references. Thus, any one consulting the index for synonyms for Acrylonitrile, the first section heading of the book, will find: cyanoethylene, propenene nitrile, or vinyl cyanide. Aldrin will be found under that heading but in the index also as 1, 2, 3, 4, 10, 10-hexachloro-1, 4, 4a, 5, 8, 8a-hexahydro-1, 4-endo-, exo-5, 8-dimethanonaphthalene, HHDN, Compound 118 or "Octalene". Allethrin may be found as such simply by looking for it alphabetically under the section headings but also in the index of compounds as dl-2-allyl-3-methyl-cyclopent-2-en-4-ol-1-onyl dl-cis-trans-chrysanthemate, dl-allylrethronyl dl-cis-trans-chrysanthemate or dl-2-allyl-4-hydroxy-3-methyl-2-cyclopenten-1-one ester of cis-trans-dl-chrysanthemum monocarboxylic acid. And so forth.

An alphabetical ordering of subjects also has certain inherent disadvantages. Chief among them is that families of related compounds whose members might otherwise be grouped under generic designations are sundered and scattered. This disability precludes also the association of all fumigant insecticides together, all systemic insecticides, all substances of plant origin, etc.

There exist several general types or groups of insecticides based on some prime mode of action or route of entrance into the insect body. Thus, a contact insecticide acts or kills when it comes in actual touch with the surface or integument of the insect. Now, if such an insecticide kills by making contact with the outer surface it may just as well have an equal action when brought in contact with an internal surface, such as that of the intestinal or alimentary tract, upon being swallowed or that of the respiratory organs on entering these. A stomach insecticide exerts its principal action when it enters the alimentary canal of the insect with that insect's normal food or in some bait attractive to it. Again a stomach insecticide may have good toxic powers by the surface contact avenue, as is true, for example, of sodium fluoride, some arsenicals, fluosilicates, etc. A fumigant insecticide acts in the form of a vapor or gas and enters the insect body primarily via the respiratory organs. It is not at all unlikely, however, that a fumigant may also, in some cases at least, pass as a gas or vapor directly through the general integument just as solid or liquid contact toxicants do. Indeed, a particular insecticide may act by any or all the routes of entry and kill in all three modes.

The several general types of insecticides may be classed further into sub-types on the grounds of nuances of toxic action. DDT, for example, kills by contact and by stomach penetration. Additionally, DDT has long persistence on a treated surface and is a contact insecticide potent enough so that an insect standing on, or otherwise touching, a surface holding a deposit of DDT may pick up by way of its integument enough of the poison to kill it. Such residual action is clearly a nuance of contact action, although the deposit, persisting for days or weeks, might just as well be taken by mouth in the case, let us say, of a leaf-eating insect as to be taken through the integument of an insect resting on a DDT-coated leaf. By contact, nicotine sulfate exerts a most potent toxic action on soft-bodied insects but it is toxic, and intensely so, for all insects when ingested. Also, nicotine sulfate being volatile, it may have a short range fumigant action by vaporization from treated surfaces or be used intentionally as a fumigant by vaporizing it in a closed space such as a greenhouse.

A new and fascinating class of insecticides—the so-called systemic insecticides—acts by various ways. They may kill by direct contact, by residual action, and by direct fumigant action. But, more subtly still, they also enter the tissues and the sapstream of plants there to serve as stomach poisons to insects feeding on the plant's tissues or juices. By metabolic transformation in a treated plant, such systemic insecticides may yield compounds decidedly more toxic than the substance applied originally. Of course, the converse may also be true in the case of other "systemics". Furthermore, some "systemics", or their metabolites, may pass from the plant as vapors in the transpiration stream and poison, as volatile fumigants, susceptible insects present within the range of their action. Some few compounds, transmitted via the blood and tissues of treated test animals, have been shown to exercise systemic action upon insects or arachnids normally feeding upon such animals as biting or sucking parasites.

Although an insecticide may be poisonous to insects by various routes of entry, the toxicity is not necessarily of the same degree by the several routes; to be lethal, penetration by one route may require a higher dosage than by another. Thus, in toxicity tests it is necessary to state precisely by what avenue of entry a toxicant has been applied to a test organism. In every instance where it has been possible to make this most significant specification it has been given in this book.

An insecticide may show wide variation in toxicity and in the speed of its action depending on the manner of formulation. Thus, if a toxicant is applied in solution the solvent may exercise a powerful influence, or if it is applied as a solid mixed with or diluted by another solid, as in a dust formulation, the diluent may strongly modify the action. Further, an insecticide's toxicity may be enhanced or potentiated in many ways by auxiliary or adjuvant agents.

Rarely are insecticide compounds used in the pure or undiluted form, a usage which would in most cases be both wasteful and overly costly. The physical state of an insecticide—for example, a viscous liquid—may preclude its use in the undiluted state, even if there are no other impediments. Thus, insecticide chemicals are ordinarily formulated in a variety of ways. They may be dissolved and/or diluted in liquid solvents, mixed with solids as dust diluents, or treated in a manner to render insoluble and hydrophobic types wettable so that they may be prepared as solid suspensions or liquid emulsions suitable for spraying. Diverse materials may have been added in formulation to act as adjuvants, synergists, stabilizers, potentiators, "safeners", emulsifiers, surface-active or detergent agents, etc. Not only may such treatments make the insecticide more easily or effectively applicable by any one of many methods but they may influence or alter profoundly the toxicity of the insecticide component for insects or related arthropods as well as for animal organisms or plants. To be fairly and usefully presented, data on toxicity should include the nature of the formulation or the physical state of the insecticide in precise form. Especially is this meaningful in any exact consideration of phytotoxic properties since in many cases the insecticide proper may be quite harmless to a plant, whereas a solvent in which it is dissolved or diluted may be decidedly harmful.

Except for fumigants, which are usually gases or easily vaporizable liquids or solids, insecticides are most usually formulated or prepared for application in the following forms:

Solutions, Emulsions, Aerosols, Dusts, Wettable powders.

An insecticide solution is simply the insecticidal chemical dissolved in a liquid in which it is soluble. The solvent and the concentration of active ingredient(s) may be such that the solution can be used directly. Usually, however, insecticides sold in solution are concentrated and must be further diluted. The simplest case, of course, is that of an insecticide dissolved in water, but the majority are not soluble in water to any great degree. Such agents may be dissolved in other solvents, such as oils or organic solvents. In turn, such solutions may be suitable for direct use or may be further diluted. (Certain solution formulations are known as emulsifiable, emulsible or emulsion concentrates, a designation which is defined immediately below.) Since insecticides must often be applied to surfaces (including the insect surface) which are not readily wettable by water or aqueous solutions, surface active agents, detergents or spreaders such as soaps, sulfonated compounds, sulfated alcohols, dried blood plasma, etc., may be added to enhance spreading, wetting or adhesion.

An insecticide emulsion indicates a liquid insecticide which is insoluble in water but which may be brought by appropriate treatment into a state in which it is suspended in water in fine droplets. An insecticide, solid or liquid, also may be dissolved in a suitable solvent (such as one of the many organic solvents) which is itself insoluble in water but which can be emulsified in water as more or less stable suspensions of fine droplets. Such concentrated solutions of insecticides in an organic solvent are the emulsible, emulsifiable or emulsion concentrates mentioned parenthetically above. Such an insecticide in concentrated solution in the organic solvent is suspended in water in the droplets of the dispersed phase of the emulsion. Emulsification may be promoted and the emulsion stabilized by use of diverse materials, soaps among them. If the insecticide is directly emulsified in water, the application of this emulsion, after evaporation of the water, leaves a deposit of the insecticide upon the treated surface. In the case of the emulsifiable concentrates, if the organic solvent is non-volatile after the evaporation of the aqueous phase of the emulsion a deposit of insecticide is left in solution in the non-volatile solvent of the concentrate. If the solvent present in the emulsifiable concentrate is, however volatile, evaporation of both the aqueous phase and the organic solvent will leave a direct deposit of the insecticide upon the surface.

An aerosol represents fine particles suspended in air as fog or mist. The term, however, is commonly used to designate an insecticidal chemical dissolved in a liquefied gas which is kept liquid under pressure in an appropriate container which may be the "tin can" of the common "aerosol bomb" or a similar but slightly more substantial re-usable container. A common substance used to dissolve insecticides for aerosol use is the refrigerant gas dichlorodifluoromethane with a vapor pressure of about 75 lbs. per inch square at 20° C. However, aerosols, in the strict sense of a cloud or mist of fine particles, liquid or solid, suspended in air may be created by burning (the so-called insecticidal "smokes" or "pyrotechnic mixtures"), mechanical atomization, heat vaporization, etc.

An insecticidal dust may represent neither more nor less than a solid (i.e., non-liquid) insecticide applied to surfaces or distributed in the form of very find particles. Most frequently, though, what is meant is a melange of an insecticide or insecticides in a finely ground solid diluent which may be any one of the various clays, earths, diatomaceous earths, talcs, chalks, finely ground organic flours such as powdered nut shells, etc. Silica gel and alumina are examples of light or "low bulk density" dust diluents, while talcs, clays, and pyrophyllite exemplify heavy or "high bulk density" diluents. To prepare an insecticidal dust, an insecticidal substance may be directly mixed mechanically with the dust diluent or may be prepared in the form of a solution (as in an organic solvent) which is then introduced as the dust is ground or tumbled. Evaporation of the solvent then leaves the insecticide in fine particles distributed in the dust.

An insecticidal wettable powder represents a finely ground or fine particulate solid or mixture of solids, among which, of course, must be the insecticide itself, prepared or treated in such a way that it may be readily "wetted" or rather dispersed as a fine suspension in water and thus applicable by spraying or dipping. Some dusts are directly wettable by the nature of the dust diluent, among them various kaolins, but others must be made wettable, and thus suspendable or dispersible in water, by adding detergent or wetting agents.

These five general classes, then, represent the more common formulations in which insecticides appear. They suggest, as may be readily surmised, various methods and instrumentalities for their application under particular circumstances. Such instrumentalities may range from the humble hand sprayer or primitive sprinkling device to elaborate fog and mist or spray-generating machines or aircraft especially adapted for insecticide dispersion. Fumigants, too, may be formulated in simple ways. For example, a certain proportion of carbon dioxide may potentiate such a fumigant insecticide as methyl bromide and cylinders under pressure may contain appropriate mixtures of these two substances.

A few other general terms appear often throughout the book; if not otherwise defined, most of these are defined operationally in the text. However, few of these general terms, among them synergist, repellent, acaricide (= miticide), pediculicide, attractant, ovicide, have a special status in that certain compounds appearing as section titles belong to classes of substances for which these terms are designations. They are defined briefly here.

A synergist is, in our sense, a chemical compound which, while itself only slightly insecticidal or even non-insecticidal, when used in association with some insecticides (chiefly the pyrethrins) greatly enhances the toxic power of the mixture (insecticide + synergist) beyond the sum of the individual toxicities of the substances in the mixture. The phenomenon of toxicity enhancement by the synergist is referred to as synergism, activation, or potentiation.

A repellent is, in our sense, a chemical compound which although itself not insecticidal, or but mildly insecticidal, makes offensive or unattractive to insects a habitat, a food plant or an animal host or other food object ordinarily sought or frequented. Repellents are customarily narrow in their action, being active in the case of only one kind or at best a few kinds of insects or related arthropods. Oil of citronella is an insect repellent of respectable antiquity.

An attractant may be said to be the exact opposite of a repellent in its action. An attractant, in our sense, draws or attracts an insect to a situation harmful or lethal to itself. The situation may be a poisoned bait, a trap, a surface treated with a powerful insecticide, etc. The attractant is presumed to act at a distance primarily by olfactory stimulation. However, purely physical attractants, for example light, sound vibrations in a certain frequency range, etc., are also known.

An acaricide is a chemical substance which shows a potent or even a specific toxic action against those insect-related arthropods which belong to the class Acarina. Among the Acarina, or acarines, are the arthropods commonly called ticks and mites. The mites encompass many genera and species of acarines which are phytophagous or plant-consuming (by sucking of the juices, chiefly) but also many genera and species which feed upon or parasitize the bodies of many animals both vertebrate and invertebrate—a type of acarine which may, thus, be termed zoöphagous. Acaricide is a term to be preferred to miticide, commonly used as a synonym or equivalent, because acaricide implies activity against acarines—a natural group of arthropods—while miticide would imply activity limited to mites. Perfectly good insecticides may also be excellent acaricides and vice versa. Nevertheless, there apparently are between insects and acarines physiological differences sufficiently striking and deep-rooted that certain chemical compounds are particularly effective toxicants for the latter and not for the former.

A pediculicide, in a strict sense, is a chemical compound effectively toxic—and even specifically toxic—for lice, and those lice members of the genus Pediculus, to which belong the lice of mankind with the exception of Phthirus pubis, the crab or pubic louse. By extension, pediculicide means louse-killer and, if we must coin words with a range so limited, let us be spared such an etymological crime as "lousicide"—a term which some have had the brass to introduce.

Ovicide refers to substances which kill eggs. In the context of this book, however, an ovicide means a compound particularly toxic to the eggs of insects or acarines.

Since the index of such a book as this is of prime importance and by its nature a key to each part of the book as a whole, a few words will be given to the index in this consideration of form as it applies to substance. Also, the index is considered here because the author discerns an error of judgment which would have proved too great to repair without additional delay of several months and a marked increment in the cost of production.

The index of the book is in two parts. One part is given over to an alphabetical listing of all chemical compound names appearing anywhere in the section headings or in the text. The second part lists the common and scientific names of all the species mentioned in the text, with the exception of the common laboratory and domestic animals which appear repeatedly under the heading, "Toxicity for Higher Animals" in each compound section. Reference is made in both parts of the index not to text page number but to the section number, it being recalled that there are one hundred and eighty-eight sections. Many individual sections are indeed quite short, made up of a few pages—from one to three at most. In these instances reference to section rather than to page may be justified since the text is in such a form that the finding of a particular item within the section is easy enough. However, some sections are quite long. In these, discovery of a particular item from the index will be harder. The system, clearly, does not take it into account that a single item may be mentioned in more than one place in any given section. The system was adopted because it was expected that the sections would be reasonably short—which most are. Some excuse for the system lies in the fact that since each section is in itself a complete treatment of the toxicity (and related) data for each compound dealt with it was thought that the interested reader would deal as a whole with the matter offered in each section. Also, the generic and specific names of plants and animals, wherever they appear in text or table, are underlined to make them stand out. The system of indexing as a whole grew from the fact that the index was made up during the critical proofreading of the manuscript text in the interest of speeding publication of the book.

The internal structure of the index in each of its parts is simple. Nevertheless, chemical terms always present special and peculiar problems. In this instance such parts of chemical names as bis-, bi-, di-, cis-, trans have validity in alphabetical ranking of terms. However, symbols for meta-, ortho-, para-, namely m-, o-, p-, whether appearing at the beginning of or internally in a term are not valid in alphabetical listing but are respected in the internal ranking of stereo-isomers if more than one are mentioned. Thus m-cresol, o-cresol, p-cresol would all be listed under "C" at their appropriate place but with respect to each other would be in the alphabetical order of m-, o-, and p-. The symbols d-, l-, and dl- for dextro-, laevo-, and dextro-laevo- also have no significance in primary alphabetization of a term.

Symbols of chemical elements appearing as components of complex compound names, for example, symbols for nitrogen, oxygen, phosphorus, selenium, sulfur (N, O, P, Se, S) are ignored in primary alphabetic listing of a term whether present at the beginning of a term, internally within the term, or both. The symbol for normal, n-, the designations primary, secondary, tertiary, symmetrical, asymmetrical, or their abbreviations pri-, sec-, tert-, sym-, asym- (as, for example, in n-butyl alcohol, tertiary butyl alcohol or tert.-butyl alcohol) are ignored in alphabetic placement of a term. The various butyl alcohols appear in proper sequence under "B" and if several appear there together, with respect to each other, they are ranked in the sequence: n-butyl alcohol, sec.-butyl alcohol, tert.-butyl alcohol. Arabic numerals occurring at the beginning, internally, or at the end of chemical terms have no validity in alphabetic listing, but are respected in the arrangement, with regard to each other, of compounds whose designations differ only in the arabic numerals. To cite some examples of these usages: such compounds as 2,2-bis-(p-chlorophenyl)-1,1-dichloroethane and bis-(dimethylamino)—fluorophosphine oxide would appear under the alphabetic heading "B" and be ranked appropriately under it by the letter (s) following the prefix, bis-, which each of them bears, the 2,2- and p- and -1,1- of the first being ignored. However, 1,1-bis-(p-chlorophenyl), etc., would precede 2, 2-bis-(p-chlorophenyl), etc., if both were listed. Also, di-(p-chlorophenyl) methyl carbinol would be found under "D" in its proper place and would precede—the p- being ignored—dicyclohexyl-ammonium, 4, 6-dinitro-o-cyclohexylphenate and dieldrin. d-Nicotine, dl-nicotine, l-nicotine would be alphabetized under "N" as nicotine but listed in the order given with respect to the polarimetric prefixes. O, O-Diethyl-O-2-(ethylmercapto)-ethyl thionophosphate appears under the alphabetic heading "D" in its appropriate place as do O,O-diethyl-S-2-isopropylmercaptomethyl dithiophosphate and O,O-diethyl-O-(2-isopropyl-6-methyl-4-pyrimidyl) phosphorothioate, listed in that order—O,O-, -O-2-, -S-2-, -O- being ignored. Of course, S, S-diethyl-O-2-(ethyl mercapto)-ethyl thionophosphate, if such a compound existed and were mentioned here, would appear under "D" but would follow in the listing its congener, O,O-diethyl-O-2-(ethylmercapto)-ethyl thionophosphate. 2, 4, 5, 4′-Tetrachlorodiphenylsulfone appears in its appropriate alphabetic place under "T"—the 2, 4, 5, 4′- being ignored—and it properly precedes tetrachloroethane. Letters of the Greek alphabet likewise are ignored in primary alphabetization. Thus β-methylallyl chloride appears under "M", succeeding methoxychlor and preceding methyl bromide.

The method of bibliographic citation and reference also has validity for the work as a whole. There is a cumulative, alphabetic list of more than 3400 references at the back of the book wherein the listing is by author(s) followed by title of book or treatise or name of periodical, volume, page number and year. The bibliographic reference numbers in the text range from 1 to 3400-odd and a reference number may appear over and over again wherever appropriate. The reference numbers as they apply to any fact, statement, numerical value, formula, chemical equation, table, etc., are set off marginally directly to the right of the matter for which they are the source. Since the text is arranged in an outline form, juxtaposition of text material and reference number(s) is direct. If a reference number (or numbers) appears alongside a fact or statement from which depend subsidiary details, statements, interpretations, etc., the reference(s) given for the leading statement remain(s) in force for unreferenced subsidiary material until a new reference number appears marginally in sequence at the right. In tabulations which bring together facts or values from many sources, each line of data carries its appropriate reference number(s). In the case of statements, interpretations, etc., which combine material from several sources, all the reference numbers of the appropriate sources are set down in the margin. Introductory statements such as head most sections under the subtitle "General", may give, to the right of the word "General," a number of references which comprise the authority for the remarks gathered there as a *precis* of descriptive, historical, and other generalities relating to the subject of the section. Some of the physical and chemical data, coming from various standard handbooks which are themselves compendia from many sources, remain "unreferenced." It seems hardly necessary to cite an authority for an atomic or molecular weight, a specific gravity, a melting point, or the shape of a crystalline structure unless there exists discrepancy or controversy with respect to such parameters. Thus, to sum up, any statement or value may be traced to its source even though, in many instances, this may rest in several references. Primary or original references have been sought as much as possible but not with exhaustive pedantry. Other treatises, compendia, and "review articles" or "annual review" type books have not been eschewed as sources.

Numerous symbols, abbreviations, and shortcuts devised *ad hoc* have been used. Save where the meaning is clearly obvious from context they are explained or defined in a brief section titled "Symbols; Abbreviations; Definitions." Such mixtures of words and chemical symbols as nicotine 2HCl for nicotine dihydrochloride, nicotine SO_4 for nicotine sulfate, ethylene Cl_2 for ethylene dichloride or 4,6-dinitro-o-cyclohexylphenol Na salt for 4,6-dinitro-o-cyclohexylphenol sodium salt or sodium 4,6-dinitro-o-cyclohexylphenate—while admittedly bad etymologically and aesthetically—have been used to save space in tabulations and text. Although the author deplores the disease of alphabetic designation exemplified by DNA, ATP, ChE, ACTH, etc., he has bowed to the necessity of space consideration.

The author greatly regrets that the multiple reference numbers are not arranged in correct numerical sequence and that there are also some lapses from alphabetical listing of the names of insects in tabulations; most of these lapses resulted from late additions of data to the text which, for various reasons, could not be resolved by rearrangement before printing.

A perusal of a representative number of the sections of the book,—in particular the sections given over to exhaustive treatment of individual insecticidal compounds—will show that, throughout, a generally consistent form has been used for the presentation of data. Many aspects of the form are self-explanatory or self-evident. Others may require interpretation, in general terms, from various stand-points. The form of each section will not exactly follow that of all others because data for one compound which would appropriately appear under a certain heading (for example "Phytotoxicity") may be entirely lacking or the heading may be inapplicable. In such a case the general topic "Phytotoxicity" would not figure in the treatment of the particular toxicant. On the other hand, for another toxicant the topic "Phytotoxicity" may be very apropos, and data upon that subject abundant. In still other instances where data on phytotoxicity would appear distinctly apropos but are, nevertheless, lacking in any precise form, the heading "Phytotoxicity" may appear with the statement that no data are available to the author or with the indication that general application to living plants for insect control indicates that at insecticidal levels the compound in question is innocuous, at least, for some plants.

After the statement of the title name of an insecticide, the listing of its synonyms, the presentation of the structural formula and molecular weight, a section customarily headed "General" gives generalities concerning the substance, its history, special abilities or disabilities it has shown in use, summary avaluations of the hazard involved, special warnings and precautions, etc. At this point a compound is characterized in brief without the presentation of precise or quantitative data.

Directly following the "General" material, physical and chemical data concerning a compound are given. These may include general description of the color, physical state, odor, taste, crystal type (if any) of the compound and may indicate any notable differences of properties existing between the substance in a state of high purity and as a technical or commercial chemical. Important physical data on melting point, boiling point, specific gravity, vapor pressure, polarimetric properties, refractive index, etc., are given, if available. Many of these data offer valuable hints on stability, persistence, and other properties. Marked attention is given to solubility; in many cases extensive tables of solubility of a compound in a wide range of solvents are supplied. This is of value as a guide to solvents suitable for concentrates, to alternate solvents which may be substituted for some which are unsuitable for reasons of toxicity, inflammability; and so on. If available, data relative to the stability of a compound in various forms and in solution are offered, with indications of halflife as a guide to possible residue hazards and time limitations of use before harvest of crop plants. Various chemical information may be listed, including such aspects as methods of synthesis, reactions undergone with various solvents and formulation additives and hydrolysis constants at various degrees of acidity or alkalinity as measured by pH. In the case of various fumigant liquids or solids data are given, if available, on the amount of the substance which may be expected to exist as a vapor in air in a stated volume under various conditions of temperature. Information on the most usual types of formulation in which the compound is used are presented. Data comparing a given compound physically and chemically with closely related compounds are emphasized when available and apropos.

The general heading "Toxicological" covers data which are most pertinently concerned with the toxicity, quantitative and qualitative, mode of toxic action, biochemical, physiological, pharmacological and pharmacodynamic properties of the compound, hazard, chronic toxicity as revealed by long-term feeding and/or exposure tests, and numerous other aspects which may be apropos generally or to a specific substance particularly. However, for simplicity, the data on toxicity included under the heading "Toxicological" are divided into three general parts: "Toxicity for Higher Animals" in all its quantitative, qualitative, acute, chronic and comparative aspects; "Phytotoxicity", similarly considering properties toxic for plants; and "Toxicity for Insects" under which are grouped, as for higher animals, quantitative, qualitative, comparative, and other data. Comparisons are made at every point where these are possible and useful. Under the general topic heading "Toxicological," special stress is given to facts and indications on hazard or toxicity for wild and game animals, terrestrial and aquatic, and for useful and beneficial insects.

The subject of the appearance of resistance to insecticides by several insect species after exposure to toxicants experimentally or in the field is dealt with as a special facet of the general physiological action of these agents. Resistance developing toward a particular toxicant is treated in the section for that compound. One general section is devoted to the fundamental subject of "acquired" resistance. Quantitative evidences of developed resistance are provided in numerous tables that deal comparatively with various strains or biotypes within an insect species in terms of such measures of relative toxicity as the LD_{50}, LD_{95}, etc., and measures of relative resistance.

Quantitative toxicological data are set forth in two complementary arrangements. This applies to each of the three general groupings of the toxicity data, namely as they relate to higher animals, plants and insects. The first of these arrangements presents grouped quantitative data of diverse origin; the second avoids such combination of data and presents data derived from one worker or group.

Under the first type of arrangement, many species are listed together sequentially in a tabular form which: provides, in general, for specification of the "route" or avenue of application of the toxicant, for example oral, sub-cutaneous, intraperitoneal, topical, inhalation or fumigation, as contact spray, contact dust, contact with a residual deposit, etc.; provides for the "dose" (as a characterization of type of dose) for example, LD_{50} (median lethal dose), LC_{50} (median lethal concentration), LD_{100} (dose yielding 100 per cent mortality), MLD (minimum lethal dose); provides for statement of "dosage", i.e., the quantity of toxicant given in stated units (micrograms, milligrams, grams, etc.) per unit of body weight (kilogram, gram, milligram or per individual organism) preferably with individual weight or average weight stated; provides a special place or column for "remarks" whereby special conditions or circumstances relative to each line of data may be given in brief. The column given to "remarks" may list, among any number of factors, such indications as exposure time, temperature during treatment, holding temperature after treatment, time of death after administration of a given dosage, vehicle or solvent, special symptomatological signs, age and condition of tested organisms, or any other useful information.

These tabulations not only group together data gathered about diverse organisms but also data derived from many sources by many methods, as the remarks and line-by-line references testify. Thus, specification of method, route, formulation, experimental circumstances, etc., is all-important in accounting for and interpreting the large variation which may be shown by data referring to one and the same species, whether this be a higher animal, an insect, or a plant. It will be apparent, the author believes, that pains have been taken, within the limits imposed by tabular method, to set forth concisely—even to the sacrifice of formal grammar and the invention of many abbreviations—pertinent circumstantial details.

The second arrangement or guise under which quantitative toxicological data are offered avoids the grouping of data from diverse sources. It reproduces directly—or in a form modified as stated in the legend—facts which derive from one worker or from collaborating workers and which ordinarily relate to but one or a few species. Such tabulations make it feasible to give more precise and full statements of experimental conditions, methods, number of replicates, statistical tests of validity, etc., than is permitted by tabulations of grouped quantitative data.

Much less opportunity for successful tabulation is given by the results of long-term feeding or exposure tests intended to measure chronic effects, accumulation in tissues, residue problems, hazard for species other than those for which the toxicant is made and, generally, effects other than those gained from tests of acute toxicity. The same is true for descriptions of various pathological manifestations, symptoms of intoxication, danger signs of toxicant accumulation in the body, histological and histopathological information, descriptions of precautionary measures, and a host of other useful and instructive indications. In the presentation of these, form has been fitted to content in many ways—chiefly semi-tabular and outline, with a heirarchy of topic headings, titles, sub-titles, etc., as may be readily appreciated by a glance at any of the longer sections and more than twenty sections devoted to "general treatments."

Wherever pertinent data are available, prominence is given to the mode whereby a toxicant generally enters the bodies of diverse living organisms and to the fate of the toxicant after entrance. By and large the most prominent methods for the application of insecticides, especially in agricultural use, are those which disperse the toxicant as a liquid spray or dust over a standing crop or the natural vegetation harboring the pest insects. Emphasis, if one may generalize, is on contact toxicity. This brings into prominence the nature and properties of the insect integument. These methods emphasize also the hazard present for creatures other than insects which may simultaneously be exposed to the insecticide. The manner whereby the insect integument mediates or impedes the entry of a toxicant into the body, the influence upon passage or failure of passage of the physical state of the poison, the nature of its formulation, the effect of solvents, of the abrasive properties of dust diluents, the thickness or degree of sclerotization of the integument and the nature of its constituents, its lipid or lipid-like or proteinaceous coats—a host of factors, structural, physical, chemical—have been the subjects of a multitude of investigations, speculations and theories.

This book does not attempt any detailed consideration of the insect integument. Still the proper interpretation of the data on contact toxicity, residual sprays and dusts, dipping experiments and dip insecticides, etc., must irresistibly draw attention to the subject of the insect integument. From the viewpoint of their bearing upon the methods and evaluations used in insecticide testing, the properties of the insect integument have been reviewed admirably by W. M. Hoskins in a recent collaborative volume edited by Harold H. Shepard and published by the Burgess Publishing Company (1958) entitled *Methods of Testing Chemicals on Insects, Volume I.*

Insecticides are pre-eminently for practical use and chiefly for use by the non-specialist. In planning this book it appeared important not only to deal with laboratory tests, but also with the precious body of data gathered from the practical field use of insecticidal chemicals, or from large scale field experiences mounted as controlled experiments but subject, naturally, to many more variables than surround the laboratory test. Many of the sections—particularly those having to do with recently developed insecticides already in use on a vast scale or with older toxicants long in use—close with a general tabulation briefly recording results or evaluations from field experiences. Such experiences give important indications of the relative merits of various insect toxicants but all judgements must be qualified strictly by the consideration that these experiences are specific and to be interpreted in the light of the variables and circumstances which are integral elements of each. A substance in controlled laboratory tests may show itself to be supremely effective as an insect toxicant for one or many species yet, if field experiences under a wide variety of naturally occurring conditions shows it to be less effective in practical insect control than a substance of lesser absolute toxicity, it must be accounted of less practical interest than other toxicants. Since a brief tabulation or *precis* cannot take account of the all-important variables and field circumstances, conclusions of the relative merits of insecticidal products should not be grounded on these indications. Such judgment should be based on the full reports.

Nevertheless, the results collected in laboratory and field have an inescapable relation. In the laboratory the methods of insecticide testing have been, and are being, progressively refined in terms of methods of controlled, effective, properly measurable application of the toxicants, among other improvements. The maximally effective use of an insecticide in the field often involves the adaptation of methods and instruments which have proved effective in laboratory toxicity tests. Precision spraying or dusting, for example, are as much to be desired in the field as they are essential in the laboratory in critical, quantitative evaluations. At the same time it should be remembered that an insecticide applied to orchards or grain-fields covering square miles by elaborate airborne devices may be used also by a horticulturist or floriculturist in a simple hand-pumped sprayer or duster.

The test of field effectiveness of an insecticide, properly applied, is full practical control (of which the optimum is, of course, elimination of the pest insects) with a minimum of danger to the user and to plants and animals. Measurements of toxicity (and thus partially or indirectly of effectiveness) made in the laboratory may use different terms or be based on quite other values. Yet, laboratory tests of toxicity tend naturally toward the determination of a practical insecticide, whether or not this is the goal. The LD_{50}, or median lethal dose, statistically speaking, for an insect form under specific conditions, may tell quite as much, and in terms as welcome, to the scientist in his laboratory as the complete elimination (LD_{100}) of a destructive pest from his field or garden achieved by that substance tells the practical user. The point is, simply, that one must not leap to conclusions solely on the basis of laboratory median lethal dose values.

The measure of toxicity most frequently employed in this book is the median lethal dose (LD_{50}) defined under specific experimental conditions, or parameters closely related thereto, such as LD_{95}, LD_{100}, LC_{50}, LC_{95}, LC_{100}, etc. This entails the need to say something about these measures of toxicity, and indirectly of effectiveness, and the methods whereby they are obtained. The methods, it goes without saying, must be appropriate, properly controlled and standardized in as many details as possible. The measures of effectiveness evoked by the methods must likewise be meaningful and subject to statistical verification of their significance.

The results or data derived from tests of toxicity are arranged, nowadays, generally in the form of a dosage mortality curve. Such a curve plots the mortality achieved in a stated period of time by a given dosage of toxicant per given unit of body weight of the test organism. A sufficient series of graded dosages (the results of which are recorded in terms of mortality per cent) yields a curve sigmoid in shape. The nearing of the asymptotic by a curve of such form to the areas of one hundred per cent mortality at one end and no mortality at the other is hard to measure and define. To find with accuracy the LD_0 and the LD_{100} calls for great replication of tests performed on large numbers of test subjects and even approximation of these values is hard indeed. In estimating them one must rely on the limited number of test individuals dying in the lower dosage range and the correspondingly few surviving in the higher dosage range. Thus individual peculiarities and idiosyncrasies become over-riding. It is far easier and more accurate to discern the dosage which yields the death of one half the number of test subjects. So, in comparisons of toxicity among substances and in determining its corollary, the differences in susceptibility to a toxicant of various species, age groups, life-cycle stages, etc., the median lethal dose (LD_{50}) has been all but universally adopted. For laboratory and domestic animals, and for vertebrates in general, dosages are expressed most commonly as milligrams or grams of toxicant per kilogram of body weight. In the case of fumigants, the median lethal concentration (LC_{50}) is generally used and is most often expressed as milligrams of toxicant per liter of air, although it may also be stated solely or supplementally as parts per million (ppm).

Some experimentalists, notably H. H. Shepard and his collaborators *(Minnesota Agricultural Experiment Station Technical Bulletin No. 120, 1937)* have taken exception to the use of the median lethal concentration value as a practical measure in testing comparatively fumigants for insecticidal power. By extension, their criticism may also be levelled at the LD_{50} generally. They have offered reasons and means for finding with statistical validity dosage values yielding more nearly complete kills of the test subjects, bringing forward argument in favor of the LD_{95} as a more practical ground for comparing toxicity. Many workers in this field report various values in their papers, for example LD_{25}, LD_{50}, LD_{75}, LD_{95}, LD_{99}.

In any case present-day tests of acute toxicity are made by applying series of graded dosages or concentrations of toxicant which yield a range of mortality values between 0 and 100 per cent of the number of test subjects. Values so obtained may be treated according to formulae and methods generalized by W. S. Abbott (*Journal of Economic Entomology 18:* 265-267, 1925). By probit-logarithmic transformation of the statistically corrected dosages and mortality per cent values the sigmoid dosage-mortality curve gives way to a dosage-mortality plot of straight line character. From plots of this type the dosages or concentrations of toxicants which may be expected to yield various percentages of mortality among the test subjects can be very well approximated. Details of method and of mathematical treatment logically applicable to comparative toxicity determinations have been provided, among others, by C. I. Bliss (*Annals of Applied Biology 37:* 508-515, 1935), F. M. Wadley (*American Association for the Advancement of Science, Publication 20,* pp. 177-188, 1943), and D. J. Finney (*Statistical Treatment of the Sigmoid Response Curve,* Cambridge University Press, 1952, second edition). Workers quantitatively testing the acute toxicity of fumigants have been for many years notably sedulous to apply careful statistical procedure and proper validity tests to their data. More recently the papers and treatises of experimentalists dealing with the toxicity of agents other than fumigants have shown increased care to state explicitly the methods whereby data have been obtained and statistically treated. Increasingly, they provide the experimental ranges of the values, standard deviation, standard error, least significant difference and other aids to interpretation of their findings.

However, standardized and accurate methods of applying or administering insecticidal substances to test insects with regard for proper controls are not as old, by any means, as are many and quite voluminous data on toxicity of insecticides, particularly those insecticides which came into general practical use during what might be called the "ancient history" of insecticides. Nowadays, and in the quite recent past, methods of exceptional ingenuity and relative ease of application have been (and continue to be) elaborated. Such methods facilitate accurate laboratory evaluations of insecticide, and would-be-insecticide, toxicity upon insect subjects. These methods show increasingly high refinement and subtlety. In miniature, of course, they reflect all the modes whereby insecticides are now applied accurately, economically, and with maximum effect on the grandest practical scale. In addition to these, delicate methods of local application to and injection into insects have been devised for purely laboratory evaluations of toxicity and mode of action. Such methods have kept pace with, and added much to, the advance of knowledge of insect physiology and biochemistry. There are, then, at hand various methods for controlled topical application and injection of insecticides to insects, precision dusting, spraying, dipping, feeding and drinking methods, ways of testing fumigant action, residual action, systemic action, effects of respiration, on enzymes and enzyme systems, on tissue microanatomy, etc. Each has its special virtues, appropriate controls, peculiar pitfalls, just as each has its proponents. All the more important, therefore, is the need to specify method and to bring forward the results of many methods in gathering general data on insecticide toxicity. Much less definite and less well explored in insecticide toxicity tests is the part played by "randomisation", sampling, and inspection or observation of test subjects during and after treatment in affecting the results achieved. It may be expected that these are factors of some importance, being among those elements of the experimental procedure that should be specified. Rarely, however, does one find them explicitly set forth.

Some general explanation of the more common methods of insecticide testing is appropriate. The unavoidable brevity imposed by the nature of the text on indications of experimental method may have made these rather cryptic. Many will ask, no doubt, what is meant when it is stated that a compound was tested upon a certain insect by application according to a certain turntable method, by some settling tower technique, by dipping or rolling or by a vacuum dusting process. Descriptions and explanations which can be given here will still not be complete. They cannot absolve the reader from looking into the reference sources for detailed descriptions if he feels need of these. Even for any general method of insecticide application there may be numerous modifications of procedure and much variety in instrumentation.

The exhaustive field test only can give the final evaluation of an insecticide in all its aspects, and of its toxicity for insects in particular, as this is reflected in the degree of control obtained. To this ultimate test, laboratory testing, carried out with high precision of method and yielding results readily reproducible, is an indispensible prelude. What follows in outline form is a short resumé of general methods presently in use in insecticide testing:

I) Topical application; direct injection:
  a) This method, which is very much to the fore at present, involves the controlled administration of toxicant in critically measured amounts, and ordinarily in suitable solution, directly to the surface of individual insects. Clearly it is a laboratory method primarily, but equally clearly it can have much to contribute to field applications of insecticides in the form of finely divided and dispersed droplets having toxicant in solution, emulsion or suspension, in the form of dusts of rather uniform particle size or as residual deposits where contact is relied upon to poison the insect. Attention is drawn to the brief section 105 of the text which offers data on spray droplet behavior.
    1) Application is made ordinarily as single drops placed upon or spread over particular chosen areas of the insect body. Thus, drops may be placed on the pronotum, on the cervical membrane, sternally or intersternally, near or far from the central nervous system or, indeed, at any chosen site. This permits evaluation of differences of susceptibility or sensitivity of the insect, if any such exist, which depend on site of application, degree of sclerotization of the integument, presence or absence of natural lipids, waxes, cuticular deposits, influence of abrasion, etc.
    2) Droplets can be delivered with precision by using needles of fine bore, carefully calibrated micrometer syringes, and various holding devices or means of anaesthesia.
  b) Much the same equipment and methods can be adapted to inject directly into the insect—under the integument, into various members, into heart, blood or other organs, into mouth or stomach—measured amounts of toxicant.
    1) Minute amounts of toxicant may be measured out by precise but essentially simple instruments. Such quantities as 0.001 to 0.01 micrograms may be delivered in small volumes of solvent or suspending fluid, for example, 0.1 to 1.0 microliters.
  c) The foregoing methods permit also consideration of the part played by various solvents in mediating or modifying the action of insecticides.
    1) Toxicity of various organic solvents such as acetone, dioxane, alcohols, etc., may be evaluated, and the part played by solvent volatility or nonvolatility, as well as many other factors, may be evaluated.
  d) Topical application or direct injection of precisely-measured and minute quantities of toxicant allow the testing of finely-graded dosages and the use of criteria other than death in studying effectiveness,

for example, doses effective in yielding particular degrees of immobility or paralysis, tremors, behavioral alterations, heart rate changes alterations of nerve action potentials, etc.

e) Topical application and injection methods are succinctly reviewed with excellent detail and bibliographic references by R. L. Metcalf in H. H. Shepard's *Methods of Testing Chemicals on Insects, Volume I*, Chapter VIII, Burgess Publishing Company, 1958.

II) Feeding and drinking methods:

a) These are the methods which come immediately to the popular mind when considerations of poisoning are brought up. Such methods of testing are a *sine qua non* for toxicants which act as "stomach poisons" upon ingestion, whether this be their sole route of effective entry or one of several routes of entry into the insect body.

1) The methods are legion and many are extremely ingenious. They have been reviewed in detail by F. W. Fisk in chapter IX of the reference cited above.

b) The test insects may have unlimited access, by feeding or drinking, to the toxicant which may be made constantly available in the food and drink by various ways. The toxicant may be mixed in or placed upon suitable food which is present in the holding cages or devices. The insects may be living in, or placed directly in, a medium in which the toxicant is present, for example: in the rearing media for fly larvae; adsorbed or absorbed by textiles in feeding tests for clothes moths, etc., in grains, flour, dried fruits and other stored products which form a habitat for the insect, for example, grain weevils; in baits rendered attractive to the insect in one way or another. The toxicant may be in liquid sirups or in fluids like plant juices or blood, drunk through membranes which simulate natural feeding situations.

c) The toxicant may be offered or administered to the insect by limited dose feeding. The toxicant may be offered in the form of deposits, pastes, coatings, etc., on the fresh leaves of suitable food plants, placed in measured amount on suitable squares or discs of acceptable leaves, as "leaf sandwiches" with the toxicant between two pieces of suitable leaves, in pellets such as bran baits. Or the poison may be given in measured doses in liquid media placed on the mouth parts, in the mouth, or introduced into the foreparts of the gastrointestinal canal.

d) These methods may be adapted as large scale semi-field tests by placing insects in large cages placed over natural food plants growing in pots or open soil and suitably treated with toxicant by various methods of spraying, dusting, coating, etc.

e) All of these tests and methods, however, carry very arduous conditions connected first with the deposit of the toxicant on the material to be eaten in measured, evenly distributed amounts so that the amount taken by the insect can be accurately measured. This may involve various planimetric techniques to discover the area eaten of such things as coated leaves so that the dosage may be estimated in terms of a known rate of deposition of the toxicant, and require delicate and time-consuming direct weighing methods, scanning methods, etc. In such feeding experiences the methods worked out for precision spraying and dusting have direct applicability as means for precise distribution of toxicant over surfaces of leaves or plant parts. Questions of natural dietary and of normal feeding habits and optimal feeding conditions are involved and play a great part in correct interpretation of results.

III) Dipping methods:

a) These methods which involve the immersion of the test insects, usually in groups or batches, in aqueous or other solutions, emulsions, suspensions, etc., of the toxicant for measured short periods really form a special case of topical application.

1) Closely related to dipping methods are those tests in which insects are rolled or shaken in dust dilutions of the toxicant or allowed to enter *ad libitum* parts of the environment over which the insecticide in suitable formulation has been dusted.

b) Plainly, the dipping and related methods are far less precise and susceptible to exacting measurements of dosage. Also it is difficult to rule out the ingestion of toxicant during the dipping process, if it is the contact effect that it is desired specifically to measure. The grooming habits of the test insects, whereby surface-applied materials are swept off by the mouth parts, are likewise to be considered.

1) Very important also becomes the treatment of the insect after its immersion—how it has been dried, whether excess moisture is blotted off, freedom of the holding cages from deposits of toxicant due to excess solution or suspension shaken from the insect surface, and a host of similar factors.

2) Consideration of harmful effects of the immersion procedure as such is necessary and such effects should be ruled out or allowed for by various refinements of the method.

c) In spite of apparent lack of precision and the presence of variables hard to control, dipping tests using adequate numbers of test subjects show a good order of reproducibility in terms of results, considered from a quantitative standpoint of dosage, exposure time, holding conditions, and so on. It is essential to administer carefully to control subjects all the treatments and manipulations undergone by the experimental subjects, save the exposure to toxicant.

1) At play here are all the factors which must be taken carefully into account in other insecticide testing methods and which should be specified in reporting results. These include: age, sex, life-cycle stage of the test subjects, nutritional state, immersion time and immersion temperature, post-treatment holding temperature and humidity, reaction time, time allowed before reading of results so that recovery from adventitious effects, such as temporary anoxia as a result of immersion in liquid, may take place.

d) Dipping methods have been reviewed in detail, and bibliography compiled, by A. H. McIntosh in chapter X of the Shepard reference previously cited.

1) Evaluation of toxicant effect after dipping application, clearly has much to indicate in terms of insecticides practically applied by this method, for example, in cattle, sheep, poultry and other dips for control of lice, ticks, mites, flesh flies, etc.

IV) Precision-spraying methods:

a) These methods as applied in the laboratory for insecticide evaluation are related directly to one of the major and universal methods for applying insecticides on a practical scale. The general methods of precision spraying are few, but special modifications and nuances are legion. They have been summarized in considerable detail and with an excellent bibliography by C. Potter and M. J. Way in chapter XI of the Shepard reference cited above. Spraying, of course, involves the dispersion by suitable instruments of a toxicant in solution, emulsion or suspension, as a cloud or mist of droplets relatively course or fine. Having created the spray or mist by suitable means, it may be applied to achieve several purposes:

1) To apply equal, similar, or comparable doses of toxicant directly to the body surface of the text insect. Plainly, this touches closely upon the methods of topical application.
2) To scatter or distribute a measured dose of toxicant in suitable solution, emulsion, or suspension over a surface area as a residual deposit with which test insects may afterward come, or be placed, in contact.
3) To distribute evenly and uniformly over the surface of something to be eaten by an insect—leaves of a food plant, other plant parts—a given dose of toxicant. This last application is done with more precision in the dispersion or distribution of stomach toxicants by settling mist methods and apparatus than by direct spraying.
4) To distribute a stated dose of toxicant uniformly over the natural habitat of the insect, or replica thereof, or over a food plant growing in field or container. This last purpose impinges upon, or merges with, the practical spray application of a toxicant when it is done with nozzles and pumps of high precision. Evaluations gained by methods so closely approaching the practical are less exact and require more judgement and discrimination for good interpretation.

b) A multitude of instruments and arrangements of instruments has been devised to achieve best, most accurately, and most directly the various purposes stated. Instrumentalities for both spraying and settling mist arrangements have been specialized for most efficient direct application of sprays to the insect body, the application of deposits to surfaces, and for both these tasks.
   1) Virtually all the instruments, or instrument groups, devised for precision spraying or the production of uniform settling mists have in common, I) an atomizing, mist- or spray-producing nozzle, II) a chamber in which insect or surface may be exposed, devised in various ways to promote mixing, take advantage of turbulence, separate different ranges of droplet size into different regions, promote even settling or distribution, etc., III) some type of reservoir, tank or cartridge in which the measured dose is placed, or from which a measured dose may be drawn, and IV) a means of exposing various kinds of test insects—crawling, flying, resting, immobilized, pinioned, etc.,—for exactly-timed intervals, and in replicate groups, to the toxicant.

c) Space does not allow any detailed description of instruments or the nature of physical factors involved in precision spraying tests. Those interested will find the details in the Shepard reference cited and its bibliography.

V) Precision dusting:

a) What has been said about precision spraying applies with equal force to precision dusting. In these methods of toxicant application the problems are those of the precise, uniform, and reproducible distribution of substances in particulate form—relatively coarse or relatively fine, uniform or diverse in particle size, crystalline or amorphous, heavy or light. However, the physical characteristics of dusts are quite different from those of solutions, emulsions or suspensions in droplet form, and are less known. Toxicants in dust form are almost invariably diluted or formulated with inert dust diluents whose properties may be highly special.
   1) As in the case of liquid sprays, dusts are applied, depending upon the mode of action and toxic properties of the toxicant, to act by direct or by residual contact, as stomach poisons after ingestion in the form of deposits on food plants, or as a result of grooming by the insect of its dusted body, or to serve a dual purpose of both contact and stomach poisoning.
   2) Whatever the method of specific application of dust toxicants, the degree of precision in terms of even distribution, amount deposited, exact dosage determination, and other quantitative considerations is much less than in the case of sprays and settling mists. Nonetheless, reasonably reproducible results have been achieved.

b) Plainly, the degree of precision in method or evaluation to be achieved by rolling, or tossing, or shaking the test insects in a quantity of the dust toxicant is not great. Much less precision attends those methods which permit the insect to enter a dusted area of the habitat or environment *ad libitum*. Still, these methods have been used and much of the older, though still valuable, data for such insecticides as sodium fluoride, cryolite and derris has been gathered by these methods.

c) As in the case of precision spraying, the desire to achieve precision dusting has brought forward numerous instrumental arrangements to yield uniform dust clouds to produce uniform deposits in several kinds of dusting and settling towers or chambers. Dust guns here take the place of nozzles.
   1) The greatest degree of uniformity achieved in distributing a measured amount of dust toxicant has come by way of vacuum dusting methods which deposit dust uniformly on all exposed surfaces of insects, food plants, cages, etc., by the instantaneous breaking of a vacuum in an appropriate test chamber or vessel.
   2) Regardless of the uniformity achieved by the dispersing apparatus, the dusting method is only as good as the methods used after application to measure quantitatively the deposit on a given area of surface or the amount ingested by an insect in the form of coated discs or squares of leaf or as leaf sandwiches with toxicant dust fillings.

d) Precision dusting techniques and apparatus have been succinctly treated by J. E. Dewey in chapter XII of the Shepard reference previously cited.

VI) Tests of fumigant insecticides:

a) Section 104 of the text presents a general consideration of fumigant insecticides. In that section may be found descriptions in considerable detail of the methods and the factors important to tests of fumigant toxicity. In addition an elegant *precis* on this subject has recently appeared and the reader's attention is drawn to chapter XIII by R. T. Cotton in the previously cited Shepard reference.

VII) Miscellaneous:

a) There have been recent new departures in the field of insecticide application and insecticide action. Among these new departures is the introduction of the so-called "systemics" or "systemic" insecticides, the subject of section 172 of the text. These require for the evaluation of their action and potency new methods and quite subtle approaches. The use of synergistic agents in insecticide formulations has proved immensely valuable and new synergists may be expected to appear in greater number. Section 171 specifically treats of the phenomenon of synergism as it applies to insecticides. Methods for the testing and evaluation of synergistic agents are given there explicitly and implicitly in the operational sense. New horizons have been opened also by the appearance and increasing elaboration of organic phosphate or "organophosphorus" insecticides.

Since the mode of action of these agents seems strongly to center upon the inhibition of choline esterase(s), *in vitro* systems for studying quantitatively the inactivation of the enzyme(s) have been devised and are important in toxicity evaluations of this "family" of toxicants. Section 134 of the text treats generally with these particular agents. Radioactive tracer methods may also be expected to come to the fore in the future. No consideration specifically of radioactive isotopes in insecticide studies has been given in this work. However an interesting review of their application in insecticide studies is offered by A. W. Lindquist in chapter VI of the Shepard reference cited above.

There remains to be considered briefly some of the important factors and variables which are all-important in their influence upon the mode of action, the toxicity and, indeed, the general behavior of insecticides as this is manifested in laboratory testings and practical field uses. Without due regard for these factors and variables, experimental data may be subject to gross misinterpretation or improper emphasis. These factors and variables are among the details which this work has sought to indicate, however briefly, in the tabulations of the experimental findings. Without these indications the tabulations may too easily appear to be a disparate melange of values showing little regularity and less coherence. More experimentalists are now explicitly considering such variables and taking the measure of their influence upon the experiential data which their studies yield. Although all these factors and variables may be found throughout the text it may serve by way of introduction to set them down as a group and consider them briefly in general terms.

Information on the variables which derive from species specificity, from inherent species difference alone, (whatever may be the physiological or biochemical basis) as these relate to insects is scarcely tapped, much less well known. Out of the thousands and thousands of insect species—to say nothing of biotypes, strains, races, varieties, etc., within those species—only a handful has formed the material for experimentation and close scrutiny. In the toxicity tabulations of this work, run down the lists of generic and specific names and consider how the same old acquaintances show up again and again in endless repetition—Anasa tristis, Apis mellifera, Bombyx mori, Melanoplus differentialis, Musca domestica, Oncopeltus fasciatus, Periplaneta americana, Anopheles quadrimaculatus. There are good reasons why this is so. There are also abundant reasons to keep in mind how limited is the penetration of our exact knowledge into this world of extraordinary organisms. As new species and genera are selected as experimental material we may expect to see many generalizations shattered or provided with interesting exceptions. This is true generally in terms of physiology, biochemistry, etc., and specifically in toxicity studies and in the insect pharmacodynamics of insecticides.

In addition to the factors making for susceptibility or resistance to the toxic action of various insecticides which are inherent in the specific nature of insects—or, for that matter, any other organism—and dependent on the particular biochemical, physiological, genetic, and structural make-up of a genus, a species, a sub-species, a variety, a biotype, a strain or an individual mutant, there are other factors which alter the activities of toxicants. Since these factors play a very great part in the variability of data on toxicity and the nature of so-called standard values derived therefrom, it seems useful to review them here. It will be noted that, in the text and tables, wherever pertinent variables have been explicitly made known by sources used, these have been indicated. Indeed, some sections are given over wholly to consideration of factors making for altered susceptibility or resistance to insecticides, among these being section 173 on temperature and insecticidal action and section 156 on "acquired" resistance or "fastness" on the part of insects toward various toxicants.

The question of those phenomena associated with individuality or "specialness", whether this relates to an individual organism or the collective individuality of a species, is too all-pervading to be usefully illuminated by the brief treatment, however succinct, which could be accorded here. These factors we will accept as given—as being of the order of nature. Others are less subtle, less all-pervading, in terms of cause and effect, and may be noted or even briefly discussed here to some useful end. The author is guided here by the order of treatment followed by C. Potter and M. J. Way of the Rothamsted Experimental Station at Harpenden, Hertfordshire, England, in chapter XI of the Shepard reference frequently cited. The bibliography provided by these authors is altogether excellent. Much of this same bibliography the author has independently explored and the specific data are embedded in the text.

I) Instar, or life-cycle stage, and age of the insect within the instar or life-cycle stage:

Susceptibility to toxicants is influenced variously by instar, life-cycle stage, age, and sex of the test insect. The degree of influence exerted may differ widely with respect to diverse toxicants. Any one of these variables may increase susceptibility to one poison and decrease it toward another.

II) Nutritional state of the test subject(s); other nutritional factors:

The nature of the food and the amount in which it is given or received alters the response of various insects toward diverse toxicants. This holds true with respect to the dietary period before testing and in the holding period after ministration of the toxicant. Myzus persicae, for example, has shown measurably different response to nicotine, used as a fumigant, depending on the plant used for rearing the aphid, namely turnip, lettuce, climbing Dahlia, Nasturtium.

III) Place of application of the toxicant on the body of the test insect:

The general organization of the integument of insects is, of course, similar over the whole of the class, Insecta. However, the disposition, nature, thickness, waxiness, oiliness, glabrousness, hairiness, wettability, etc., of the cuticular layer of the integument alone, may differ sharply as between species, between life-cycle stages or instars, and between body regions. If the insect is or can be sprayed, for instance, over-all by an effective contact insecticide or toxicant these differences are not too important save as their algebraic summation may determine the overall effective dose. Quite different, however, is the situation in tests whereby the dose may be deliberately localized. And this fact achieves practical importance with regard to toxicants intended for use as residually toxic deposits or films. Susceptibility of the individual insect has been found to vary markedly depending upon the region of the body where a given test dose is applied. This may be manifested by difference in the LD_{50} of a given toxicant for different application sites, time required for the production of a given response—death or otherwise—and in many other ways. At any given place of application, the physical state of the toxicant, the solvent used, and the environmental circumstances attending the application may alter the result.

IV) Physical condition and state of the toxicant; vehicle or medium of application:

Especially in the case of a poison applied as a solid, either by contact or by mouth, do the particle size and nature of the crystal or shape of the particles affect the result in terms of the susceptibility or resistance of the insect. The type of vehicle or medium is of great importance as it enhances or promotes entry of the poison to the sensitive regions or systems of the test subject, makes the toxicant more palatable or acceptable, quiets or inhibits mechanisms which might effect the regurgitation of an intaken poison or promote or retard the rate of passage through the gut, synergizes with the toxicant, or in any way alters or affects the natural barriers to the entry of foreign substances. Thus, of course, the nature of a formulation may influence deeply the activity of any given insecticide. Surface active agents, pH of the medium, protective adjuvants added to retard degradation or alteration of the toxic molecule, all may affect the quality and intensity of the response of the test subject. In the case of contact poisons working as residual deposits, the texture or nature of the surface has an effect on toxicity both in terms of influence on the toxicant itself and the effect it has on the adequacy of contact of the test subject with the poisonous deposit.

V) Deposit level and toxicant concentration:

In the case of contact sprays, contact dusts, and residual deposits or films, made either by application of dusts, emulsions, suspensions or solutions, these factors influence toxicity as this is revealed by measurements of test subject mortality. Usually, when a stated volume of dissolved poison is administered, by direct contact or as a residual deposit, toxicity increase is a direct function of increased concentration of toxicant. Over the mortality range, or most of it, probit-mortality and log-concentration relation is linear when graphed. Oil-borne toxicants used as sprays yield an enhanced mortality with increased deposit level but this effect may not follow in the case of water-borne toxicants. The so-called run-off point of the solution, suspension, or emulsion may be such that any increase of amount applied beyond that point has no effect in enhancing the amount of poison held on the insect surface. In residual deposits, too, a level may be noted below which there is no response on the part of the subject, and a level above which no increase in toxicant deposit will enhance the response. With regard to this deposit range the nature of the surface holding the deposit is an important factor. Depending upon the particular toxicant, application in a concentrated or in a diluted form may yield an optimum toxic effect. Technique of application is a factor in this last consideration. In the case of tests by settling mists, dusts, and spray methods, particular attention must be accorded to levels of deposit and concentration.

VI) Exposure time; reaction time, or inspection time, or test-"reading" time:

The stretch of time during which a test subject can continue to receive toxicant from its surroundings, from its food, from its own surface, or however, is termed the exposure time. The time passing between the start of application or administration of a toxicant and the moment when the result of the test is "read" or determined in terms of the response of the test subject is the reaction time. This latter becomes important when a subject is exposed to a toxicant for a given period then removed to a place where there is no further exposure to additional toxicant, but where the subject may be held for some additional time before the response is determined, or the results of the test read. If the test involves study of the effects of contact of the subject with a residual deposit, then exposure time and inspection time are the same, if contact of subject and toxicant is maintained until response determination. Sufficient prolongation of exposure time or reaction time will yield, eventually, a maximum effect for the dosage received. Speed of action is the inverse of the time needed for the effect of a particular dose to reach its maximum. It is not the time needed for a particular dose to yield a stated response.

The action of a toxicant may be weighed from the standpoint of its power to yield a certain effect on the test subject, such as producing immobility, excitement, death, etc., regardless of time taken to produce the effect. Determining a toxicant's action from this standpoint sets aside variables such as speed of action or uptake. On the other hand, the determination of a poison's action may be made in full consideration of action speed or uptake speed. Each type of assessment of toxicant action carries its own special conditions. In the first case highest, maximum, or end-point effects must be determined, and thus exposure time and reaction time must be sufficiently long to yield the end-point. However, if this length of time is so great as to permit starvation, adventitious changes, or to outrun the normal longevity of the subject, plainly, other assessments of action are needed. However, the results obtained by the first type of determination or assessment are those more generally meaningful and valid. Results based on reaction and exposure times of an intermediate duration are set by the action speed. In case of residual films results may be affected or changed by influences which alter speed of uptake from the film or speed of reaction to the amount of toxicant taken. To gain the fullest knowledge of toxic action and data sufficient for valid comparisons, studies should be made to yield time-mortality data for various dosages of toxicant as well as data for dosages applied in terms of set exposure or reaction periods.

VII) Temperature and toxic action; humidity and toxic action:

Tabular and other materials indicating the nature and extent of temperature effect on insecticide toxic action are included in section 173. At this point a few remarks may serve to generalize those data. Temperature effect on the action of insecticides on insect test subjects is particularly marked when studied in terms of the temperature at which the test insects are held after treatment. These effects, have shown up, particularly when studied after administration of toxicants by mouth and by direct contact with the insect body, in the form of differences in toxicity of the toxicant and in the time needed to yield one or another form of response. In the case of many poisons higher holding temperatures after treatment with toxicant yield higher mortalities—within physiological limits, of course. Although some data are offered in section 173, less is known about the influence of environmental temperature in the pre-treatment period. Variation in the size of the temperature coefficient depends on many things—the toxicant itself, the specific nature of the test subject, the conditions of the test, and the physical state in which the toxicant is administered. Whether the temperature coefficient is positive or negative depends, apparently most usually, on the insecticide itself, although conditions of test and type and state of test subject no doubt have some influence. Different environmental temperatures for the treated insects, then, yield differences in relative and absolute toxicity of a toxicant, considered alone and in combination with other toxicants or with various forms of the one poison. DDT and some of its close relatives are notable in showing a negative temperature coefficient, in terms of post-treatment temperature, for a number of commonly used test insects. But this effect is by no means common to all the so-called chlorinated hydrocarbons. Temperature during the course of treatment also influences the rate of response to a toxicant. If, however, an insect is treated with a toxicant at a given temperature and held at the same temperature during the post-treatment period the effect is not essentially different when that given temperature obtains only during the post-treatment period.

Humidity of the insect environment before treatment with a toxicant—provided humidity is not such as to affect adversely the vitality or physiological condition of an insect—seems to play no part in affecting the toxicity of a substance. Humidity has been said to influence the toxicity of residual deposits during the exposure period but studies of this effect of humidity are few, incomplete, and not particularly ingenious. Far more is known about the very real effects and problems of humidity on the phytotoxicity of insecticides.

VIII) Other factors:

The amount of toxicant absorbed by some mosquitoes and the housefly, exposed in a space misted with kerosene solutions of pyrethrins, has been shown to be related to the movement activity of these flying insects. Active flying movement apparently increased the dosage of toxicant received upon the body. It is also reported that movement of actively crawling insects enhanced the toxicity of insecticidal deposits. The self-grooming activities of cockroaches and flies which have been dusted, or have picked up insecticidal dusts from dusted environments, have been shown to enhance the mortality by adding a gastrointestinal intoxication to the contact toxicity. Obviously, this would be true in the case of a toxicant relatively low in toxic effect by contact, but good in stomach poisoning power. Most insects, at least as adults, groom themselves and those doing so most persistently and actively might be expected to show the foregoing effect more than others. Effects have been described in toxicity tests of insecticides as due to intensity of light, palatability, repellent nature of insecticide or formulation, anaesthesia, intestinal motility or intestinal stasis, aeration (in fumigant insecticide tests), admixture of carbon dioxide with certain fumigant vapors and impurities in the toxicants used.

In these prefatory remarks many useful indications have not been touched on at all. The author again wishes to draw the attention of the reader to those sections of the text which deal with certain general aspects of insecticides and their action or with natural chemical "families" of insecticides. A number of such sections treat of quite new agencies as yet scarcely explored, for example, section 6 on antibiotic and antimetabolite effects in insects. The general problem of the hazard of insecticides for useful and beneficial insects—for bees, for pollinators, for insects parasitic on noxious species—is approached operationally through tabulations of known data in section 12. Although this section deals chiefly with bees, many of these observations have general validity beyond the immediate horizon of the apiculturist.

With respect to toxic effects of insecticides applied on a grand scale, few good critical studies have been made. In section 183 on Toxaphene®, however, there has been set down a *precis* of some excellent field experiential data gathered from happenings in several southern cotton-growing counties where insecticides distributed on a grand scale, combined with certain circumstances of weather, yielded very drastic effects on wildlife. Such a study, though limited, serves as a working model and a guide.

Certain sections in the text may seem odd, for example, section 44 on the effect of insecticides on cytochrome oxidase. Why single out this enzyme and devote to it a section, however brief? Simply because these data presented as a coordinated unit were gathered by one investigator on a sizeable number of different insecticides and lent itself to such unique presentation. The vastly richer documentation on the effect of certain insecticides on choline esterase is not so treated and a reader of the text may be baffled by an apparent major omission. However, reflection will suggest that it is primarily the organic phosphate insecticides and the carbamates and carbamic acid esters which inhibit the biochemical action of the esterases for acetylcholine and its chemical relatives. Thus, it is in the general sections, namely sections 27 and 134, that the nature and meaning of this enzyme inhibition by insecticides is explored. Again, why section 145 on phytotoxicity which deals with a handful of species of garden shrubs and trees? The same reasons obtain as those offered for the section on cytochrome oxidase—a coordinated block of comparable data given by one assiduous worker on purely horticultural woody plants. Elsewhere, under the sections given over to specific insecticides, abundant phytotoxicity data may be found.

The best way to learn the uses of this work, if the author may so suggest, is a careful perusal of the subject index to appraise the general range of its subject matter. Then, a consideration of a few of the insecticides—such as DDT, Parathion, Pyrethrins, Rotenone, for which there are varied and abundant data—will give a good idea of the general internal arrangement and method of presentation of data followed throughout. Not all the same headings appear in every section. Plainly, an insecticide used solely to control body lice or a substance to repel chiggers from the human body present little scope for any data on phytotoxicity; no such section may be expected to appear even if only to report the absence of specific data.

Hindsight sees deficiencies which even the most earnest application and arduous thought while work was in progress did not bring to notice. For these deficiencies there is real regret; but there is hope that sufficient usefulness, if not excellence, is at hand so that readers will be moved to suggest corrections for deficiencies, omissions, and sins of commission. If the work has value and is found to deserve at some future time to be reissued in expanded and ameliorated form to keep it abreast of a burgeoning subject, then the deficiencies of the present may be changed into the virtues of the future.

WILLIAM O. NEGHERBON
Loyola College, Baltimore

ACKNOWLEDGMENTS

Such value as this compilation may have derives wholly from the immense body of original data on which it depends. The data which the book presents are the fruit of the original observations and creative experiments of a host of scientific workers. The data, and the accounts of the methods by which they were gathered, are to be found in a multitude of publications, domestic and foreign. The *apologia* for this work is its purpose of bringing these far-scattered facts into a more readily accessible and useful form.

To the best of his ability, the author has yielded full credit in every instance to those whose work he has used. The great number of his "creditors" is evident in the table of references. A compiler cannot make complete repayment to those whose work and acumen in experiment are the substance of all his own effort. By setting the work of his "creditors" accurately, and without bias, however, in the context of other works of a like, a comparable, or a contrasting nature, an author may give substantial (although only partial) recompense to his sources. Until such time as some ready form of coding and sorting of facts becomes universally accessible, compendia will have their reason for being.

A compiler may be ambitious to assemble an entire field of knowledge. His task may be to labor upon a mountain of facts, reducing it to a well-concentrated hill. He must judge his materials with care, choosing from his sources the essential, without distorting the intention or losing the nuance of interpretation offered by the originator.

In preparing many sections of the book, the author found indispensable many data, both published and unpublished, or available only for special purposes, given to him with exemplary generosity by several firms and corporations through their research agencies and representatives. To these the author is greatly indebted. Each one is appropriately mentioned in the table of references and cited at every point in the text where such data appear.

The author finds another obligation deeply pleasant to make known. This obligation he owes to those who have supported, encouraged, aided, and made possible his efforts, and those who have taken personal part in the preparation of this book. They have contributed more than their measure to whatever usefulness or excellence this work may have. For its many faults, already known or yet to be discovered, they are in no way responsible—these faults are wholly the author's and for them he shoulders the blame.

Those, then, to whom the author is immediately, deeply, and equally obligated are:

Dr. JOHN W. HEIM and Dr. GEORGE KITZES who, representing officially the Wright Air Development Center, Air Research and Development Command, United States Air Force, made possible the entire conception, preparation, and presentation of this work and followed it with unfailing and friendly patience, comprehension, and suggestion. Through Drs. Heim and Kitzes the author salutes respectfully the United States Air Force for that largeness of view and generosity which undertakes the support of far-ranging scientific activities.

Those officers and staff members of the National Academy of Sciences—National Research Council who advanced and helped in every way the actual preparation of the manuscript for publication.

Messrs. JAMES MAUK, PAUL GRIFFIN, and ROBERT SIEBERT who worked tirelessly, with undaunted patience and good humor, to proofread expertly the entire work and who played an essential part in preparing the indexes.

Dr. WOLFGANG von OETTINGEN and Dr. LLOYD HAZELTON, of the National Institutes of Health and the Hazleton Laboratories respectively, who encouraged the author by their personal kindness and exceptional scientific integrity through numerous difficult circumstances which they will remember.

The faculty authorities of Loyola College, Baltimore, who through several months of the Fall Semester of 1958-59 were happy to condone the absence of the author from his duties for two days a week spent in Washington in the final work of preparation of this book for printing.

W. B. SAUNDERS COMPANY, publishers, in the persons of their expert and understanding agents whose professional advice, friendly, experienced judgment, and unmerited praise greatly helped the author to bring this work before the public.

To each and all of them the author gratefully offers his enduring thanks.

WILLIAM O. NEGHERBON
Loyola College, Baltimore

CONTENTS

Note: The Table of Contents of this work is made up of two classifications.

The section titles which have been underscored deal with certain general aspects of insecticides and their action, or with certain natural "families" of insecticidal compounds, for example: Insecticidal Fumigants, Synergists and Synergism, Organic Phosphates, Resistance to Insecticides.

The section titles which have not been underscored list chemical compounds of insecticidal interest, each compound being the title of a section. Mainly, the preferred chemical designation of a compound has been used. However, where names made up *ad hoc,* for example: Malathion, Parathion, Lindane, etc., have passed into general use, such names are listed in the Table of Contents.

Almost every one of the compounds dealt with has from one to many synonyms of common or chemical derivation. These are listed in the general index of compounds at the end of the book. In the general index of compounds most of the valid synonyms are given, without, however, any attempt being made to include there the multiplicity of trade or formulation names under which a great many of these chemical substances appear before the public.

SECTION Page

1. ACRYLONITRILE 1
2. ALDRIN 4
3. ALLETHRIN 13
4. ALLYL BROMIDE 20
5. ANABASINE 22
6. ANTIBIOTICS; ANTIMETABOLITES 24
7. ARSENIC AND ARSENICALS 25
8. ARSENIC TRIOXIDE 37
9. ARSENOMETHANE DISULFIDE . . . 41
10. AZOBENZENE 43
11. BARIUM SILICOFLUORIDE 45
12. BEES AND INSECTICIDES; BENEFICIAL INSECTS AND INSECTICIDES 47
13. BENZENE HEXACHLORIDE 53
14. BENZYL BENZOATE 75
15. BIS-(p-CHLOROPHENOXY)-METHANE 76
16. 2,2-BIS-(p-CHLOROPHENYL)-1,1-DICHLOROETHANE (DDD; TDE) . 79

SECTION Page

17. 2,2-BIS-(p-CHLOROPHENYL)-1,1,1-TRICHLOROETHANE (DDT) 85
18. BIS-(DIMETHYLAMINO)-FLUOROPHOSPHINE OXIDE 124
19. 2,2-BIS-(p-FLUOROPHENYL)-1,1,1-TRICHLOROETHANE (DFDT) 127
20. BIS-(MONOISOPROPYLAMINO)-FLUOROPHOSPHINE OXIDE . . . 128
21. BORAX 131
22. BUTOXY POLYPROPYLENE GYLCOLS 400 and 800 132
23. 2-BUTOXY-2′-THIOCYANODIETHYL ETHER 134
24. BUTYLPHENOXYISOPROPYL CHLOROETHYL SULFITE 139
25. CALCIUM ARSENATE 143
26. CALCIUM CYANIDE 146
27. CARBAMATES AND CARBAMIC ACID ESTERS AS INSECTICIDES 148
28. CARBON DISULFIDE 151
29. CARBON TETRACHLORIDE 156

SECTION Page

30. CHLORDAN(E) 161
31. p-CHLOROBENZYL-p-CHLOROPHENYL SULFIDE 175
32. CHLOROBROMOPROPENE 176
33. CHLOROMETHYL-p-CHLOROPHENYL SULFONE 177
34. p-CHLOROPHENYL BENZENE SULFONATE 178
35. p-CHLOROPHENYL-p-CHLOROBENZENE SULFONATE 179
36. p-CHLOROPHENYL PHENYL SULFONE 182
37. CHLOROPICRIN 185
38. CLOTHING IMPREGNANTS VS. CHIGGERS (TROMBICULIDS) . . . 189
39. COAL TAR DYES 189
40. COPPER ARSENATE (BASIC) 190
41. COPPER CYANIDE 191
42. CRYOLITE 192
43. CYCLETHRIN 196
44. CYTOCHROME OXIDASE, (EFFECTS OF INSECTICIDES ON) . . 198
45. D-D® 199
46. DERRIS (Also see Section 157) 201
47. DIBUTYL ADIPATE 203
48. DIBUTYL PHTHALATE 205
49. p-DICHLOROBENZENE 206
50. 1,1-DICHLORO-2,2-BIS-(p-ETHYLPHENYL) ETHANE 208
51. DICHLOROETHYL ETHER 210
52. 1,1-DICHLORO-1-NITROETHANE . . 212
53. 2,4-DICHLOROPHENYL BENZENE SULFONATE 215
54. DI-(p-CHLOROPHENYL) METHYL CARBINOL 216
55. DICYCLOHEXYLAMMONIUM-4,6-DINITRO-o-CYCLOHEXYLPHENATE 220
56. DIELDRIN 222
57. DIETHYL 2-CHLOROVINYL PHOSPHATE 241

SECTION Page

58. DIETHYLDITHIOCARBAMIC PHOSPHORODITHIOIC ANHYDROSULFIDE, O,O-DIISOPROPYL ESTER 242
59. O,O-DIETHYL O-2-(ETHYLMERCAPTO)-ETHYL THIONOPHOSPHATE 244
60. O,O-DIETHYL-S-2-ISOPROPYLMERCAPTOMETHYL DITHIOPHOSPHATE 251
61. O,O-DIETHYL O-(2-ISOPROPYL-6-METHYL-4-PYRIMIDYL) PHOSPHOROTHIOATE 252
62. O,O-DIETHYL O-(4-METHYL-7-COUMARINYL) THIONOPHOSPHATE 261
63. O,O-DIETHYL O-(3-METHYLPYRAZOLYL)-(5) PHOSPHATE 262
64. O,O-DIETHYL O-(3-METHYLPYRAZOLYL)-(5) THIOPHOSPHATE . . 264
65. O,O-DIETHYL S-PROPYL MERCAPTOMETHYL DITHIOPHOSPHATE 265
66. O,O-DIISOPROPYL S-ISOPROPYL MERCAPTOMETHYL DITHIOPHOSPHATE 265
67. DILAN® 266
68. DIMETHYL-1-CARBOMETHOXY-1-PROPEN-2-YL PHOSPHATE . . 269
69. O,O-DIMETHYL O-3-CHLORO-4-NITROPHENYL THIONOPHOSPHATE 270
70. O,O-DIMETHYL O-(2-CHLORO-4-NITROPHENYL) THIOPHOSPHATE 275
71. O,O-DIMETHYL O-2,2-DICHLOROVINYL PHOSPHATE 278
72. 5,5-DIMETHYLDIHYDRORESORCINOL DIMETHYLCARBAMATE . 280
73. DIMETHYL PHTHALATE 283
74. O,O-DIMETHYL-2,2,2-TRICHLORO-1-HYDROXYETHYL PHOSPHONATE 284
75. 2,4-DINITRO-6-SEC.-BUTYLPHENOL 289
76. 4,6-DINITRO-o-CRESOL 291
77. 2,4-DINITRO-6-CYCLOHEXYLPHENOL 298

SECTION Page
78. DINITROPHENOLS 303
79. DIPHENYLENE OXIDE 308
80. DIPHENYL SULFONE 308
81. ENDRIN 310
82. EPICHLOROHYDRIN 320
83. 1-ETHOXYMETHYL-1,1-DI-(p-CHLOROPHENYL) CARBINOL . . 323
84. ETHYL ACETATE 324
85. ETHYL-4,4′-DICHLOROBENZILATE 325
86. ETHYLENE CHLOROBROMIDE . . . 328
87. ETHYLENE DIBROMIDE 330
88. ETHYLENE DICHLORIDE 334
89. ETHYLENE OXIDE 342
90. ETHYL FORMATE 347
91. 2-ETHYL-1,3-HEXANEDIOL 349
92. N-(2-ETHYLHEXYL)-BICYCLO-[2.2.1]-5-HEPTENE-2,3-DICARBOXIMIDE 350
93. ETHYL-p-NITROPHENYL BENZENETHIONOPHOSPHONATE . . 351
94. FLUORINE, FLUORIDES, FLUOSILICATES, FLUOALUMINATES. 360
95. FURETHRIN 365
96. HEPTACHLOR 366
97. HEPTACHLOROPROPANE 375
98. HEXACHLOROETHANE 377
99. HEXACHLOROPROPENE 378
100. "HEXAETHYL TETRAPHOSPHATE" 379
101. HYDROGEN CYANIDE 383
102. HYDROXYPENTAMETHYL FLAVAN 389
103. INDALONE® 391
104. INSECTICIDAL FUMIGANTS 392
105. INSECTICIDE SPRAYS, DROPLET BEHAVIOR 411
106. ISOBORNYL THIOCYANOACETATE 412

SECTION Page
107. N-ISOBUTYL UNDECYLENEAMIDE 415
108. ISODRIN 416
109. 1-ISOPROPYL-3-METHYL-PYRAZOLYL-(5)-DIMETHYL-CARBAMATE 421
110. 2-ISOVALERYL-1,3-INDANDIONE . 423
111. LAURYL THIOCYANATE 427
112. LEAD ARSENATE 430
113. LIME-SULFUR 436
114. LINDANE 437
115. LONCHOCARPUS (Also see 157) . . . 450
116. MAGNESIUM ARSENATE 451
117. MALATHION 451
118. MERCUROUS CHLORIDE 465
119. METHANESULFONYL FLUORIDE . . 466
120. METHOXYCHLOR 467
121. β-METHYLALLYL CHLORIDE 475
122. METHYL BROMIDE 477
123. METHYLENE CHLORIDE 485
124. METHYL FORMATE 486
125. METHYL PARATHION 488
126. MITICIDES OR ACARICIDES 491
127. MITIN® 502
128. MOSQUITO LARVAE; BODY LICE (TESTS OF INSECTICIDES AGAINST) 504
129. NAPHTHALENE 505
130. NICOTINE 508
131. NORNICOTINE 520
132. OCTAMETHYL PYROPHOSPHORAMIDE 521
133. n-OCTYL SULFOXIDE OF ISOSAFROLE 534
134. ORGANIC PHOSPHATES (ORGANIC PHOSPHORUS ["ORGANOPHOSPHORUS"] INSECTICIDES) 536
135. ORGANIC THIOCYANATES AND THIOCYANOACETATES 570

SECTION Page

136. OVIPOSITION INHIBITORS FOR MUSCA DOMESTICA 575
137. PARA-OXON 577
138. PARATHION 580
139. PARIS GREEN 598
140. PENTACHLOROPHENOL 600
141. PETROLEUM OILS, MINERAL OILS, TAR OILS, ETC. 603
142. PHENOTHIAZINE 609
143. 1-PHENYL-3-METHYL-PYRAZOLYL-(5)-DIMETHYL-CARBAMATE 612
144. PHOSPHORUS 617
145. PHYTOTOXICITY 618
146. PIPERONYL BUTOXIDE 619
147. PIPERONYL CYCLONENE 623
148. 2-PIVALYL-1,3-INDAN(E)-DIONE 625
149. PLANTS (INSECTICIDAL) 628
150. PROPYLENE DICHLORIDE 631
151. PROPYLENE OXIDE 633
152. n-PROPYL ISOME 634
153. 2-n-PROPYL-4-METHYL-PYRIMIDYL-(6)-DIMETHYL CARBAMATE 635
154. PYRETHRINS I, II; PYRETHRUM . . 636
155. REPELLENTS 651
156. RESISTANCE 652
157. ROTENONE; "ROTENOIDS" 661
158. RYANIA, Active Principle = RYANODINE 673
159. SABADILLA 676
160. SESAMIN 682
161. SODIUM ARSENATE 685
162. SODIUM ARSENITE 686
[illegible] SODIUM FLUORIDE 689
164. SODIUM FLUOROACETATE 694
165. SODIUM FLUOSILICATE 696

SECTION Page

166. SODIUM SELENATE 699
167. STROBANE® 702
168. SULFUR 708
169. SULFUR DIOXIDE 710
170. SULFURYL FLUORIDE 712
171. SYNERGISTS; SYNERGISM 716
172. SYSTEMIC INSECTICIDES 722
173. TEMPERATURE AND INSECTICIDAL ACTION 729
174. TERMITES (REPELLENTS AND INSECTICIDES FOR) 732
175. 2,4,5,4′-TETRACHLORODIPHENYL-SULFONE 733
176. TETRACHLOROETHANE 734
177. TETRACHLOROETHYLENE 736
178. TETRAETHYL DITHIONOPYRO-PHOSPHATE 738
179. TETRAETHYL PYROPHOSPHATE . 740
180. TETRA-n-PROPYL DITHIONO-PYROPHOSPHATE 747
181. THALLIUM SULFATE 750
182. 2-THIOCYANOETHYL ESTERS OF C_{10}-C_{18} ALIPHATIC ACIDS 752
183. TOXAPHENE® 754
184. TRICHLOROACETONITRILE 770
185. TRICHLOROETHANE 773
186. TRICHLOROETHYLENE 776
187. TRIETHYL TIN HYDROXIDE AND ITS ESTERS; INSECTICIDAL ACTIVITY 778
188. WILFORDINE 780

BIBLIOGRAPHY 781
INDEX OF SCIENTIFIC AND COMMON NAMES OF INSECTS, OTHER ANIMALS AND PLANTS MENTIONED IN THE TEXT 831
INDEX OF CHEMICAL COMPOUNDS 843

SYMBOLS; ABBREVIATIONS; DEFINITIONS

$[\alpha]_{y^\circ}^{x^\circ}$ Indicates the polarimetric properties of an optically active substance under standard conditions of temperature.

↑ Indicates: Increased, increasing, enhanced, elevated, raised, enlarged.

→ Used in any other manner than that universally employed in chemical equations, means, as may suit the context: Yielded, gave, led to, brought about, served as, resulted in, produced.

† = mortality, kill, killed, dead, dead at.

/ = per, as in mg/day (milligrams per day), lbs/acre (pounds per acre), mg/insect (milligrams per insect), etc.

♀ = female. The symbol doubled (♀♀) = females.

♂ = male. The symbol doubled (♂♂) = males.

$<$ = less than, smaller than, lower than, or, to suit the context, diminution in a quantity, quality, attribute, dimension, etc.

$>$ = more than, greater than, higher than, or, to suit the context, increase in or enlargement of a quantity, quality, attribute, dimension, etc.

μg/ = microgram(s) per, for example g/k (microgram(s) per kilo), μg/insect (microgram(s) per insect), etc.

$d_{y}^{x^\circ_\circ}$ = specific gravity at the temperature, in degrees centigrade, indicated by the superscript referred to water at the temperature, in degrees centigrade, indicated by the subscript.

$n_D^{x^\circ}$ Refers to the light refractive properties of a substance.

AcChE = acetylcholine esterase.

Act. Ingred. = active ingredient(s).

ACTH = adrenocorticotropic hormone.

ADP = adenosine diphosphate.

ATP = adenosine triphosphate.

Av. = average, for example, av. wgt. = average weight.

b.p. = boiling point.

bu = bushel(s), an English and American unit of volume (dry material).

$\bar{c}$ = with.

C ; C° = centigrade; degree(s) centigrade.

ca = *circa* or approximately, about, near, nearly.

Ch E = choline esterase. Often found as cholinesterase.

Chlordane - non R = chlordane non-resistant, or, conversely, susceptible or sensitive to chlordane.

Chlordane - R = chlordane resistant, or refractory (usually in a relative sense) to chlordane.

Chlordane - S = chlordane susceptible or sensitive; the equivalent of chlordane non-R.

cm² = square centimeter(s) or centimeter(s) square.

CNS = central nervous system (in the sense of brain and spinal cord).

Comm., comm. = commercial or commercial grade, referring to the degree of purity of a product as it appears customarily in commerce or trade.

Comp., comp. = compound(s).

Conc., conc. = concentration; referring to the relative amount of a substance (ordinarily stated in per cent) in solution in, suspension in, or mixture with another substance.

Contact Spray In this work refers to an insecticide in solution or suspension in a liquid, applied in such a way that the insects are directly wetted in whole or in part.

Cpd. compound(s). Also see Comp., comp.

CSMA = Chemical Specialties Manufacturers Association.

ct = cutaneous. Here specifically indicates the application of a substance to the body of an animal by placing it in contact with the surface of the skin or integument.

CTC = concentration to control. In this work, the concentration of an insecticide needed to yield practical field or "economic" control.

D (in headings), *d* (in text) = dextro-rotatory; referring to the polarimetric properties of the substance. Associated always with the name of a specific chemical compound, for example *D*-(or *d*-) nicotine.

DDT-non R = DDT non-resistant or, conversely, DDT susceptible or sensitive to DDT.

DDT - R = DDT resistant, or refractory (usually in a relative sense) to DDT.

DDT - S = DDT susceptible or sensitive; the equivalent of DDT non-R.

DL (in headings), *dl* (in text) = dextro, laevo and signifies a racemic mixture of dextro- and laevo- rotatory racemers of a substance; refers to the polarimetric properties of a substance. Always used with the name of a specific chemical compound, for example *DL*- (or *dl*-) nicotine.

EC = effective concentration. As, for example, EC_{50}, EC_{95}, etc., signifying effective concentration for 50%, effective concentration for 95%, etc., of a group of tested subjects statistically significant in number. Refers to a concentration effective in producing some specific result, for example, death, paralysis, increase or decrease in respiratory rate, etc.

ED = effective dose; that amount of a substance which applied in a particular way is sufficient to evoke a certain response in the tested subject.

Emuls., emuls. = emulsion.

Emuls. Conc., emuls. conc. = emulsible or emulsifiable concentrate. Refers to a concentrated solution of a substance in some solvent, this concentrate being employable in making up emulsions in water.

Est., est. = estimated, for example, estimated dosage, estimated LD_{50}, etc.

Exp., exp. = exposure, or exposed to or at. Thus: 2 hr. exp. = 2 hour or 2 hours' exposure, exp. 80° C = exposed at 80° C, exp. DDT = exposed to DDT, etc.

F ; F° = Fahrenheit; degree(s) Fahrenheit. Refers to a specific scale of temperature measurement.

f.p. = freezing point.

ft. = foot or feet (plural); an American and English unit of linear measure.

ft² = square foot or feet; foot or feet square.

ft³ = cubic foot or feet; foot cube or feet cube.

Fumig, fumig = as a fumigant. Indicates application of a toxicant by fumigation, i.e., as a gas, vapor or vaporisable liquid or solid in the atmosphere contained in the test vessel, chamber or space.

Gal., gal. = gallon, gallons. Where otherwise unspecified, as, for example, gal. U.S., gal. Imperial, the United States gallon as a measure of liquid volume is meant.

Hgt., hgt. = height.

Hr., hr. = hour; 60 minutes.

Hrs., hrs. = hours.

I = instar. For example, 4 I = 4th instar. An instar refers to the interval between moults in an insect's life cycle. Thus, the fourth larval instar refers to the period between the third and fourth larval moults.

I_{50} Equivalent to ID_{50}, q.v.

ID_{50} = inhibition $dose_{50}$; in this work means that dose or amount of a substance yielding, under particular conditions, 50% inhibition of choline esterase(s) or acetylcholine esterase(s) in a given reaction system. As, for example, $ID_{50,\ 30\ min}$, indicates a dosage yielding the 50% inhibition in 30 minutes.

in. = inch or inches, an English and American unit of linear measure. 12 in. (inches) = 1 ft (foot).

in² = square inch or inches; inch (inches) square. 12 in.² = 1 ft² = 1 square foot.

Ingred., ingred. = ingredient(s), for example, as act. ingred. = active ingredient(s).

Inh, inh = inhalation, by inhalation, as inhalant, and refers to intake of a substance by inbreathing, in the case of air-breathing vertebrate test subjects, or, in the case of insects or other arthropods, the application of a substance as a gas or vapor with intake presumed to be in whole or in part by means of the respiratory apparatus.

Inj, inj = injection or by injection. Refers to the introduction of a substance by mechanical means into (beneath the surface of) the body of the test subject. Injection may be at various levels and into various sites, as for example, subcutaneous, intramuscular, intravenous, intraparenteral, etc.

Intermed., intermed. = intermediate.

intra - abd. = intra-abdominal. Refers to the introduction or injection of a substance into the lumen, space, or cavity of the abdomen. Essentially equivalent, in the case of a vertebrate animal, to intraperitoneal introduction or injection.

ip = intraperitoneal. Refers to the introduction or injection of a substance into the peritoneal space or cavity of a test subject (by definition a vertebrate animal). Thus, administration of a substance by the peritoneal portal.

IT = immobilization threshold. Refers, in this work to that amount of a substance or toxicant which, applied to a test subject or a group of test subjects in a particular way, is just sufficient to yield cessation of movement.

iv = intravenous. Refers to the introduction of a substance into the body of an animal by direct injection into a vein, or into the venous circulation.

KD = "knock down", or knocked down, i.e., (in the present context) reduced to immobility, or reduction to immobility. Used, by extension, to mean paralyzed or paralysis; inability to move normally. Does not imply necessarily the death, instant or eventual, of the organism knocked down by the treatment causative of the "knock down". Not placed in quotation marks when used in any table.

"KD" see KD. The quotation marks are added, if the abbreviation is used in the text (as opposed to use in a table), because of the general lack of precision in the idea of "knock down".

KD_x (where x = a subscript) For meaning of KD, see the definition under that abbreviation. The subscript applied to KD may mean, if it is a number without further specification, e.g., KD_{50}, KD_{10}, "knock down" of 50% or 10% of the tested subjects. If there is specification, e.g., $KD_{10\ min}$ or $KD_{24\ hrs}$, the degree of "knock down" in 10 minutes or in 24 hours would be meant.

L (in headings), *l* (in text) when used in the chemical name of a compound, e.g. *L*-NICOTINE or *l*-nicotine, *L*-ANABASINE or *l*-anabasine, = laevo- (or levo-) rotary: Refers to the polarimetric properties of a substance. Not to be confused with the abbreviation for liter(s) or litre(s).

l = liter(s), litre(s).

Lab, lab = laboratory, as, for example, lab strain, lab biotype meaning a laboratory strain, a laboratory biotype.

Lb., lb. (plural: Lbs, lbs.) = pound (plural: pounds) one of the English and American units of weight. One pound = 16 ounces.

LC = lethal concentration. For example, the lethal concentration of carbon tetrachloride vapor in air, for the cat, has been given by one worker as 90 milligrams per liter of air; the lethal concentration of DDT in water, for tadpoles, has been given as 0.1 part per million by some workers. The examples cited indicate the concentration of the substances named, in air and water respectively, which will kill at least one of a group of test subjects.

LC_x (where x = a subscript as, for example, LC_{50}) lethal concentration$_x$. Thus LC_{50} or LC_{10}, for instance, signify amounts of a substance in a medium such as air, water, etc., which will prove fatal respectively to 50% or 10% of a statistically significant group of test subjects, exposed suitably thereto. The LC_{50} of chloroform as an example, is given by one worker as 27.8 milligrams per liter of air for the mouse, exposed for 7 hours to the test medium, with death occurring in 8 hours.

LC_{xy} (where x = a subscript number, e.g. LC_{50}, and y = a further designation such as 24 hrs. 2 days, 10 min.) See definition given for LC_x. Such additional subscript designation as 24 hrs., 2 days, 10 min. ordinarily indicates that the result, for example 50% mortality, is achieved in the time or period specified. This may be quite different from exposure time. However, in many instances it is difficult to know if the time designation refers to the exposure period or the time in which the stated result, such as 50% kill or mortality, was achieved after a particular exposure period.

$\frac{LC_x}{LC_{x'}}$ (where x, x' are subscripts such as 50, 90, 100 etc.) = LC_x divided by $LC_{x'}$, for example LC_{50} divided by LC_{90}. See the definitions given for LC, LC_x and LC_{xy}.

LD = lethal dose. The amount (dose) of a substance which will kill or prove fatal to a given animal or organism. An imprecise designation. See LD_x, MLD, LD_{XY}.

LD_x (where x = a subscript number, for example, LD_{10}, LD_{50}, LD_{75}, LD_{100}) = lethal dose$_x$. Thus LD_{10}, LD_{50}, LD_{75}, LD_{100} signify amounts of a substance which kill respectively 10%, 50%, 75%, 100% of a statistically significant group of test animals (ordinarily 10 or more individuals). The designation LD_0 may seem paradoxical; where used it indicates a dose, in a series of graded doses, which uniformly kills none of a group of test subjects.

$\frac{LD_x}{LD_{x'}}$ = LD_x divided by $LD_{x'}$, for example LD_{50} divided by LD_{100} (see the definition given for LD_x).

LD_0 See LD_x.

LD_{10} See LD_x.

LD_{50} See LD_x.

LD_{75} See LD_x.

LD_{90} See LD_x.

LD_{95} See LD_x.

LD_{99} See LD_x.

LD_{100} See LD_x.

LD_{xy} (where x = a subscript number, e.g., LD_{50}, and y a further subscript designation such as 24 hrs., 2 days, 1 week, etc.) See the definition given for LD_x. Such additional subscript designation as 24 hrs., 2 days, 1 week indicates that the result shown as LD_x occurred in the time (y) specified. Thus $LD_{50,\ 24\ hrs.}$ means the amount (dose) of a substance which yielded 50% mortality in 24 hours of a group of test subjects, individually treated with the amount stated.

LL = lethal level. For example LL_{50}, indicates a degree or rate of application of a substance productive of 50% mortality of the exposed subjects.

LR = lethal range.

L deposit$_x$ (where x = a subscript number, e.g., L deposit$_{50}$, L deposit$_{100}$) = lethal deposit$_x$. Thus, L deposit$_{50}$, L deposit$_{100}$, indicate, respectively, the amounts of a substance, measured as a deposit on a surface, for instance milligrams per square centimeter, which will kill 50% or 100% of a group of test subjects which have access to, or are exposed to, the treated surface. Refinement may be had if the time necessary for the given degree of kill to occur is specified as, for example, L deposit$_{50\ 24\ hrs}$.

L Time = lethal time. Refers to the time required for a dose of a drug or toxicant, sufficient, by definition, to kill a test subject eventually, to produce mortality. As L Time$_{50}$, the time necessary for a given dose of a drug or toxicant to yield mortality of 50% of a statistically significant group of test subjects.

μg = microgram(s), microgramme(s).

M = mole(s), or molar (in reference to a solution).

m = meter(s) or metre(s).

m^2 = square meter(s) or meter(s) square.

m^3 = cubic meter(s) or meter(s) cube.

MED = minimum effective dose; e.g. MED_{95} minimum effective dosage for 95% of the test subjects. See ED.

Medium In reference to a route of application, indicates that the toxicant or drug is applied to the test subject by way of the environment or surrounding material, for instance, application of a toxicant or drug to a fish by dissolving or suspending the substance in the water in which the subject lives.

mg/k = milligram(s) per kilogram(s) of body weight.

Min, min. = minute(s).

Mixt., mixt. = mixture.

MLC = minimum lethal concentration, namely, that least amount of a material in solution in a liquid, as a solid in a solid diluent, as a gas or vapor in air, which will yield, on appropriate exposure, the death of at least one individual of the tested group of subjects.

MLD = minimum lethal dose, i.e., the smallest of a series of graded doses or amounts which will kill one individual of a group of test subjects.

MLD_{100} = the least dose or amount of a substance which when given to each of a group of subjects yields 100% mortality. An ambiguous concept which appears here and there in published data under the designation MLD_{100} and which is essentially equivalent to the much clearer LD_{100}, q.v.

mm = millimeter(s) or millimetre(s).

mm^2 = square millimeter(s) or millimeter(s) square.

mm^3 = cubic millimeter(s) or millimeter(s) cube.

mm Hg$^{(x)^0}$ Indicates vapor pressure in millimeters of mercury at the temperature designated in the superscript. (Here, for generalization, given as $(x)^0$.)

m.p. = melting point.

MTD = minimum toxic single dose.

MTL = mean tolerance limit(s).

NAIDM = National Association of Insecticide and Disinfectant Manufacturers.

no. = number(s), e.g., no. (number) of subjects tested, no. (number) of tests, etc.

OCI = Official Control Insecticide.

or = oral. Refers to the introduction of a substance into the body of an animal by mouth.

oz = ounce or ounces (16 ounces = one American or English pound [as unit of weight]).

Pd, pd = period. Refers to a stretch of time, e.g., test period, feeding period.

Post-treat; post-treat = post-treatment, i.e., after treatment.

ppm = part(s) per million. Refers to concentration.

Pt(s); pt(s) = pint(s). An English and American unit of volume. Two pints = one quart; 8 pints = one gallon.

pwdr = powder or as a powder; in the powdered condition or state.

PNS = peripheral nervous system. See CNS.

R = range. The lower and upper limits of a series of values.

Ref(s) = reference(s), in the sense of published data cited in the bibliography.

Rel. = relative. For example relative toxicity, i.e., the toxicity of one substance with reference to another as a standard and expressed as unity.

Rel. Tox. = relative toxicity.

R.H. = relative humidity.

Route = means or avenue of application of a drug or toxicant to a test subject.

RR = railroad, e.g. railroad car, RR car.

sc = subcutaneous. Refers to the introduction of a substance into the body of an animal by injection directly beneath the skin or integument.

S.E. = standard error. Used in the statistical sense.

sec. = secondary.

sensu stricto = in the strict sense or meaning.

So. = southern, e.g., southern army worm.

sol. = (as may suit or fit the context) solubility, soluble, solution.

sp. = species (singular).

Spec., spec. = special.

spp. = species (plural).

Spray Refers to the application of a substance in solution or suspension in a liquid medium in the form of a cloud or mist of droplets by using a suitable dispersing apparatus or method. Also, by extension, used to indicate a substance suitable for application by, or intended to be applied by, spraying.

std. mix. = standard mixture.

Susp., susp. = suspension, in suspension, as a suspension.

Tech., tech. = technical, in the sense of the technical grade of a substance. Connotes a degree of chemical purity less than that of a material designated chemically pure, or of reagent grade.

Temp, temp = temperature.

tert. = tertiary.

TL_m = median tolerated limit.

Tolerance Limit_{50} = greatest dosage tolerated with 50% survival of a group of test subjects large enough to have statistical validity.

Topical With reference to method of application or administration of a substance indicates the placing of the drug or toxicant directly upon the surface or integument of the test subject(s).

Toxic C = toxic concentration.

Turnover When used as a characterization of dose, indicates that amount of a drug or toxicant which will cause a fish to float in the water with the ventral surface, or belly, uppermost.

U.V. = ultraviolet. Refers specifically to ultraviolet (U.V.) light.

veg. = vegetable (e.g., veg. oil).

v.p. = vapor pressure.

Vs., vs. = versus, against, used against.

Wett. pwdr. = wettable powder. Refers to a powdered substance prepared in such a way as to be readily wetted or suspensible in water.

Wgt. = weight

Wk., wk. = week(s).

Wt. = weight. See wgt.

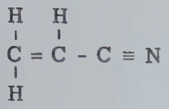
yd = yard. An English and American unit of length. One yard = 36 inches or three feet.

yd^2 = square yard(s) or yard(s) square.

yd^3 = cubic yard(s) or yard(s) cube.

1

ACRYLONITRILE (Cyanoethylene; Propenenenitrile; Vinyl cyanide)



$\underset{H}{\overset{H}{C}}=\overset{H}{C}-C\equiv N$

Molecular weight: 53.06

GENERAL (Also see Fumigants; Trichloroacetonitrile.)

Acrylonitrile is considered one of the best available fumigants for insects. It is effective against stored prod- 2629
ucts insects at concentrations of 0.7 - 1.4 lbs/1000 bushels. In the vacuum fumigation of tobacco at 1.25 lbs/ 616
1000 ft^3, acrylonitrile is more penetrating than hydrogen cyanide, HCN, and almost as toxic. It has proved ef- 181
fective in fumigation of boxed products at 0.25 lb/1000 ft^3. As an effective "spot-fumigant" it may be dispensed 353
as a liquid in suitable amounts into crevices, "dead spots," and in mill machinery where grain or flour may
accumulate.

PHYSICAL, CHEMICAL

A colorless, inflammable liquid; m.p. -82°C, b.p. 77.3 - 77.5°C; $d_{4°}^{20°}$ 0.797, $d_{4°}^{25°}$ 0.801 (liquid); d 1.8 (gas; air = 1), $n_D^{25°}$ 1.3885; v.p. 105 mm Hg$^{25°}$; maximum existing as vapor in air at 68°F = 15 lbs/1000 ft^3; flash point 4°C, 32°F; explosive mixture in air = 3.05% lower limit, 17% upper limit; solubility = 7.4 parts in H_2O 100 parts, 3.4 parts H_2O dissolve in acrylonitrile 100 parts; miscible with most organic solvents; 1 mg/l = 461 ppm, 1 ppm = 0.002168 mg/l; 569 cc = 1 lb, 6.7 lbs = 1 U.S. gal.

TOXICOLOGICAL

Highly poisonous. Maximum allowable concentration for man is placed at 20 ppm. The low vapor pressure 2221
permits the "spot" use of acrylonitrile without wearing a respirator. Vapors are irritating, lacrimatory, self- 55
warning.

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage mg/k	
Mouse	or	LD	>20, <72	2210
Mouse	ip	LD_{50}	15	2210
Rat	or	LD_{50}	93 (81 - 106)	2910
Guinea Pig	or	LD_{50}	50	2907
Rabbit	ct	LD_{50}	250	2907

Animal	Route	Dose	Dosage		Remarks	
			mg/l	ppm		
Rat	inh	LC_{50}	1.1	500	4 hr exposure.	480
Rat	inh	MLC	1.38	635	4 hr exposure; death in 8 hr.	866
Dog	inh	MLC	0.24	110	4 hr exposure; death in 4 hr.	866
Monkey	inh	—	—	90	4 hr exposure; transient effect.	616
Pin Perch*	medium	—	—	20	deleterious, toxic.	690

*A marine fish.

PHARMACOLOGICAL, PHARMACODYNAMIC, PHYSIOLOGICAL, ETC.

1) Mode of toxic action:
   a) Action is similar to that of cyanide. Evidence suggests the in vivo hydrolysis of acrylonitrile to inorganic 868
   cyanide. Sodium nitrite, $NaNO_2$, increases resistance to acrylonitrile and has been used as an antidote. 869

2) Symptoms of poisoning in man, higher animals:
   a) Early symptoms in man are: Salivation, eye and nose irritation, skin flush, rapid respiration. 868,869
   b) Other symptoms are: Weakness, light-headedness, headache, nausea, sneezing, abdominal pain, vomiting, unconsciousness, asphyxia and finally death. 2221
   c) Lethal doses in animals yield a temporary paralysis and then convulsions as prelude to death. 868,869

PHYTOTOXICITY

1) Tests of acrylonitrile at doses as high as 12.5 lbs/1000 ft^3 using seeds of 13 common vegetables showed no harmful effects. 1200

TOXICITY FOR INSECTS

1) Cimex lectularius: Fumigation in 12 liter flasks at atmospheric pressure; exposure 5 hrs; temperature 25°C. 2622

	Acrylonitrile alone (LC_{95} - LC_{100})	Acrylonitrile + CCl_4 (1:1) (LC_{95} - LC_{100})
Nymphs	3 - 4 mg/l	7.5 mg/l
Adults	<2.5 mg/l	7.5 mg/l
Eggs	<2.0 mg/l	6.0 mg/l

2) Acrylonitrile vapor is only slightly less toxic than hydrogen cyanide, q.v., for Cimex lectularius. 2629

3) Toxicity for some stored products insects, exposed in the adult stage in empty fumatoria (100 ft^3) at 70° F: 2005

Insect	Exposure Time 2 Hours		Exposure Time 6 Hours	
	LC_{50} (mg/l)	LC_{95} (mg/l)	LC_{50} (mg/l)	LC_{95} (mg/l)
Acanthoscelides obtectus	3.0	5.5	1.1	2.0
Oryzaephilus surinamensis	3.5	6.5	0.8	1.4
Rhizopertha dominica	2.5	4.0	0.8	1.4
Sitophilus granarius	4.5	8.0	2.0	2.9
Sitophilus oryzae	2.5	6.5	1.0	1.8
Stegobium paniceum	3.0	7.0	1.7	2.5
Tribolium confusum	6.5	11.0	3.0	4.9
Zabrotes pectoralis	2.0	4.0	1.4	2.1

4) Comparative toxicity under conditions of empty flask exposure and exposure in the presence of whole wheat grain; exposure time 24 hrs at 72°F and atmospheric pressure; adult insects: 616 2629

Insect	Dosage for 100% Kill (mg/l)	
	in empty 20 l flasks	in 20 l flasks with 0.5 bu of wheat
Sitophilus oryzae	1.6	8.0 (ca 0.7 lb/1000 bu)
Tribolium confusum	5.0	16.0 (ca 1.4 lb/1000 bu)

a) In presence of wheat, a non-inflammable mixture of acrylonitrile and CCl_4 (1:1) is almost as effective at similar dosages as acrylonitrile pure.
b) If treated wheat is milled without air washing, milling quality is unfavorably affected while baking quality is improved. Acrylonitrile absorbed by wheat readily leaves under air washing.
c) The killing action on insects is prolonged for 5 hours after end of exposure in presence of wheat.

5) Dosages needed for 50% and 95% mortality of adult insects exposed 24 hrs in wheat at various depths. Wheat contained in 28 l cans, 14.5 in. high, 12.5 in. diameter, 30 lbs whole wheat/can, spread 8 in. deep with free space above grain surface of 6.5 in.; 80°F: 2009

Insect	Depth in wheat	Dosage (mg/l) for	
		LC_{50}	LC_{95}
Sitophilus granarius	surface	< 2.6	< 2.6
	2 in.	2.6	4.0
	5.5 in.	4.0	6.8
Tribolium confusum	surface	4.6	6.6
	2 in.	8.2	13.6
	5.5 in.	13.8	19.0*

*0.67 cc/0.5 bu.

6) Acrylonitrile + CCl_4 (1:1) vs. Lasioderma serricorne (larva) exposed in baled Turkish tobacco at various depths: 181

Dosage oz/1000 ft^3	Exposure hrs	Temperature °F	% Kill at Depths of: 1 in.	2 in.	5 in.	7 in.	9 in.	Control	
16	72	71.1	100	90.8	83.6	84.8	86	8.8	Atmospheric Pressure
20	72	72.6	100	100	100	100	100	8	
28	48	76	100	100	100	100	100	0	
28	24	81	100	100	99.6	99.6	99.6	5.6	
32	24	76	100	100	100	100	100	3.2	
64	3	73 - 76	100	100	100	100	100	10.4	Pressure = 28 in.Hg
32	3	75 - 86	100	100	100	100	100	1.6	
24	3	72 - 78	100	100	100	100	100	6.4	
20	3	73 - 82	100	100	100	100	100	2.4	
16	3	70 - 79	99.4	99.7	99.7	100	100	8	
12	3	70 - 77	100	100	100	100	100	7.2	
8	3	70 - 77	81	77	66.9	70.4	63.7	6.4	

7) Toxicity for naked eggs (23-26 hrs old) and 3rd instar larvae of Dacus dorsalis exposed 2 hrs at 71° - 80°F in empty vessels: 255

Nitrile	Eggs		Larvae	
	LC_{50} mg/l	LC_{95} mg/l	LC_{50} mg/l	LC_{95} mg/l
Acrylonitrile	1.2	1.6	$<$ 1.2	1.6
Acrylonitrile + CCl_4 (1:1)	3.7	11	1.7	4.9
Acetonitrile	44	75	$>$82.4	-
Chloroacetonitrile	1.2	1.5	$<$ 1.3	$<$ 1.3

a) For Tribolium confusum chloroacetonitrile is of the same order of toxicity as acrylonitrile, LC_{50} for each, as fumigant, being: $<$2mg/l. Chloroacetonitrile is less toxic than di- and tri- chloroacetonitrile. 2629

8) Residual action; duration of toxic effect:

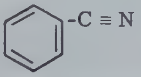
a) Flour, 3 in. deep, exposed in open dishes over paper wet with acrylonitrile at 2 ml/375 g flour yielded 100% kills of adult Tribolium confusum, exposed at or below the surface, for 1 day and 50% - 100% kills for 2 days. 2853

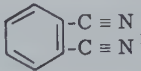
9) Acrylonitrile and other nitriles compared for toxic effect vs. insects exposed for 24 hrs at 80°F and 70% - 80% relative humidity: 615

Nitrile	Minimum Dosage Yielding 100% Kill (mg/l)	
	Sitophilus oryza (adult)	Tribolium confusum (adult)
2-Chloroacetonitrile	0.6	1.2
2,2-Dichloroacetonitrile	0.68	3.4
2,2,3-Trichloropropionitrile	0.7	2.1
ACRYLONITRILE	0.8	1.21
2-Chloroacrylonitrile	1.0	1.63
Trichloroacetonitrile	1.43	4.29
2,2,3,4-Tetrachlorobutyronitrile	1.46	2.19
2-Chloropropionitrile	1.6	7.49
3-Chloropropionitrile	1.7	2.28
2,2,3-Trichlorobutyronitrile	1.98	1.98
2,2,4-Trichlorobutyronitrile	2.0	2.72
2,2-Dichloropropionitrile	2.42	6.05
2,3-Dichloroisobutyronitrile	3.63	4.84
4-Chlorobutyronitrile	4.4	3.3
3-Chlorobutyronitrile	6.9	6.42
Isobutyronitrile	7.61	11.4
N-Butyronitrile	7.96	7.96
2,2-Dichlorobutyronitrile	11.7	11.7
Propionitrile	11.7	27.4
Acetonitrile	27.4	27.4
2-Chloroisobutyronitrile	8+*	8+*

*No kill at this dosage.

10) Aromatic nitriles:

a) Benzonitrile,  , acts as a stomach poison but not as a contact poison for insects. 356,351,3055

b) o-Dicyanobenzene (phthalonitrile),  is a highly toxic stomach poison for caterpillars and dipterous larvae. m-Dicyanobenzene is non-toxic for insects. 2127

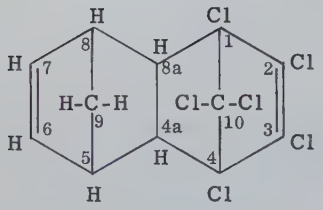
c) Toxicity increases from benzonitrile to phenylacetonitrile thereafter decreasing to phenylpropionitrile to increase again, with desaturation, to styryl cyanide. Cyclohexenylallyl-acetonitrile is potently toxic for lice. The chlorination of benzonitrile at the para- position yields good louse-killing compounds. 2884 918 2179 3032

d) Toxicity of aromatic nitriles for some insects: 351,353,356

Nitrile	LC_{50}, ppm		LD_{50} (contact) $\mu g/cm^2$	
	Musca	Sitophilus	Blattella	Oncopeltus
Benzonitrile	400	1700	0	0
Benzyl cyanide	310	660	35	0
o-Chlorobenzyl cyanide	270	580	55	0
p-Chlorobenzyl cyanide	640	200	80	320
2,4-Dichlorobenzyl cyanide	550	110	430	0
3,4-Dichlorobenzyl cyanide	750	590	100	0
β-Phenylpropionitrile	780	940	105	0
Styryl cyanide	1300	107	120	0

2

ALDRIN (1, 2, 3, 4, 10, 10-Hexachloro-1, 4, 4a, 5, 8, 8a-hexahydro-1, 4-endo,-exo-5, 8-dimethanonaphthalene; HHDN; Octalene; Compound 118.)



Molecular weight 365

GENERAL

Aldrin is an insecticide of the cyclodiene group, a family of highly chlorinated cyclic hydrocarbons, among which in addition to aldrin are: Chlordane, dieldrin, endrin, heptachlor, isodrin and toxaphene, q.v.

PHYSICAL, CHEMICAL

When highly purified, a crystalline, colorless solid; in commercial or technical grade, a buff, tan, or brown, waxy solid above which when in bulk at > 77°F small amounts of supernatant liquid may be present; not flammable; m.p. (pure) 104°C, m.p. (commercial grade) not < 90°C; v.p. 6 x 10^{-6} mm Hg$^{25°C}$ (less volatile than lindane, q.v., above 32°C, more volatile than lindane below 32°C); insoluble in H_2O; soluble in most organic solvents (most paraffinic, aromatic, and alkylated solvents holding at least 2.0 lbs of technical aldrin per gallon): 2812

Approximate solubilities at 77°F, 25°C

Solvent	% (wt) in saturated sol.	g/100cc solvent	Solvent	% (wt) in saturated sol.	g/100cc solvent
Acetone	58	66	Kerosene	26	24
Amyl acetate	31	30	Methanol	6	4
Benzene	67	83	Methylcellosolve	13	14
n-Butanol	11	9	Methylethyl ketone	26	24
Carbon tetrachloride	66	105	Pentane	3	3
Deobase oil	18	16	Summer Diesel	26	25
Dipentene	57	61	Toluene	75	98
Ethanol	7	5	Turpentine	60	70
Ethylene dichloride	72	104	Winter Diesel	32	31
Fuel oil	26	25	Xylene	73	92
Isopropyl alcohol	5	3	Water	<0.1 ppm	-

Odor (technical grade) is mild, "chemical," pine-like on heating; density = 13.0 - 13.8 lbs/gal at 68°F, ca 97 lbs/ft^3; aldrin content of technical product = 82% by wt (minimum) of which 95% is pure product; free acid < 0.1% by wt as free HCl; emulsibility potential good; stable in storage and in presence of alkalis, weak or dilute acids, metallic chlorides; persistence of toxic residues is less than in any other chlorinated insecticide except lindane; compatible with most available agricultural chemicals including fertilizers, herbicides, fungicides and other insecticides; may be used in presence of alkaline soils, lime, lime-sulfur, Bordeaux mixture and other basic materials; unaffected, unless acidity is below pH 3.0, by combination with acid insecticides.

Formulations: Wettable powders (aldrin 20% - 40%), dust concentrates (aldrin 75%), granules (aldrin 1%- 25%), emulsifiable concentrates (aldrin 2 lbs/gallon), dusts of low aldrin (%) content.

Residues on crops: Said to be low, < 0.1 ppm at harvest, if used in strict accordance with directions.

TOXICOLOGICAL

1) General remarks: Acute toxicity is relatively high. Aldrin is absorbable via the gastrointestinal canal, by inhalation, and through the skin, the last constituting the greatest occupational hazard. 2812 2345

2) Recommended precautions: 2345
   a) Special training of spraying workers.
   b) Use of protective clothing, rubber gloves, respirators in mixing and handling of concentrates.
   c) Avoidance of spray rebound.
   d) Daily, thorough shower baths for mixing-plant and spraying workers.
   e) Immediate and complete washing of contaminated skin.
   f) Prevent contamination of all food for men and animals.

3) Acute symptoms:

a) Man: Hyper-irritability, depression, vomiting and nausea, headache, convulsions (onset in 1-4 hours), 129
coma. Death within 24 hours. 2221

b) Mammals: Central nervous excitation with reflex excitability, convulsions, bradycardia, vaso-depression, 2231
miosis.

4) Chronic toxicity: Nature of symptoms unknown for man. In animals symptoms are: Loss of appetite and weight, nervousness and irritability. 353

5) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage	Remarks	
Rat	or	LD_{50}	67 mg/k		2231
Rat♂	or	LD_{50}	54.2 ± 6.2 mg/k		169
Rat♀	or	LD_{50}	56.0 ± 5.3 mg/k		169
Rat	or	LD_{50}	10 mg/k	As aldrin (2.5% wett. pwdr. Strauss process).	169
Rat	or	LD_{50}	44 mg/k	As aldrin (2.5% wett. pwdr. thermal process).	169
Rabbit	ct		15-25 mg/k	2 min. immersion, wett. pwdr. formulations yield anorexia, nervousness, wild activity, spasms lasting 3-10 minutes.	1713
Rabbit	ct	LD_{50}	< 5 mg/k	As repeated, daily exposures.	1952
Rabbit	ct	LD_{50}	< 150 mg/k	Single, acute exposure to dry aldrin.	1952
Chicken*	or	LD_{50}	10 - 15 mg/k		111
Chicken**	or	LD_{50}	25.5 mg/k	In acetone; death in 12 hrs-5 days.	2824
Goldfish	medium	LC_{80}	0.032 ppm	10 day exposure, 20°C, 15 l aquaria.	828,100
Goldfish	medium	LC_{50}	.02 ppm	" " " " " " "	828,100
Goldfish	medium	LC_{10}	.01 ppm	" " " " " " "	828,100
Goldfish	medium	Turnover	.05-.1 ppm	24 hrs exposure.	828,100
Minnow	medium	LC	.01 ppm	For some individual subjects.	828
Minnow	medium	LC_{50}	.018 ppm	10 day exposure in 15 l aquaria.	828

*3 and 6 weeks old.
**1 week old.

6) Toxicity for higher animals; feeding experiments:

Animal	Dosage	Feeding Period	Effect	
Rat	5 ppm		None.	1953
Rat	25 ppm		Liver damage.	1953
Rat	50 ppm		Gross effects.	1953
Rat	75 ppm	6 months	Aparently normal.	353
Rat	25 ppm	6 months	None.	129
Dog	0.5 mg/k/day		No deaths.	1953
Dog	1.0 mg/k/day	109, 344 days	Death of 2 test animals at days stated.	1953
Dog	5.0 mg/k/day	21, 22 days	Death of 2 test animals at days stated.	1953
Chicken	25, 50, 100, 200 ppm		100% kill of 3 and 6 week olds.	111
Mouse	50 ppm	2 weeks	Hyperexcitability, diarrhoea, tonic convulsions, death. Liver enlarged with hypertrophy and cloudy swelling.	75

7) Sub-chronic and chronic toxicity:

a) General: Calves over-wintered successfully when fed on hay sprayed at rate of 1 lb/acre; cows gave aldrin-free milk when fed on hay sprayed at rate of 0.5 lb/acre. 353

b) No harmful effects were noted among workers in aldrin manufacturing plants when proper precautions were followed. 2548

c) Sub-chronic toxicity in chickens 1 week old at start of exposure: 2825

Concentration ppm	Mean Kill (%)	Mean wt Gain Survivors at 7 wk ♂	Mean wt Gain Survivors at 7 wk ♀	Mean Food Consumption g/bird 1 week	Mean Food Consumption g/bird 2 week	Conversion Efficiency to 3 wk age
50	22.5	709.1	611.9	126.7	184.1	2.16
25	2.5	814.9	679.3	138.7	199.9	2.06
12.5	0	855.3	688.6	155.3	200.5	2.18
6.25	0	851.6	691.9	131.7	189.9	2.08
0.0	0	842.9	703.6	133.4	191.6	2.01
LSD* 5%		52.1	43.7	36.7	37.3	1.17
LSD 1%		69.0	57.7	50.5	51.4	1.61

*Least Significant Difference.

8) Toxicity for wild birds, Quail and Pheasant, subjected to feeding tests, with 10 birds tested at eacn dosage level:

a) Adult birds:

Bird	Aldrin Fed		Aldrin Consumed (mg/k)		Kill	Survival Time (days)
	%	ppm	daily	total	%	
Quail	0.5	5000	12.0	46.4	100	4
"	.25	2500	11.8	46.3	100	4
"	.125	1250	5.5	20.8	100	4
"	.0625	625	2.2	9.1	100	4
"	.01	100	0.7	3.3	100	5
"	.005	50	1.9	9.7	100	5
"	.001	10	0.9	7.3	100	8
"	.0005	5	0.5	20.0	100	42
Pheasant ♂ *	.01	100	1.7	13.8	100	8
" ♀ *	.01	100	1.4	50.4	100	36
Quail Control**	—	—	—	—	4.1	154
Pheasant " **	—	—	—	—	3.6	100

*5 subjects of each sex.
**96 quail, 108 pheasants.

b) Young birds, continuous feeding:

Bird	Number	Age at Start days	Test Length days	Aldrin in Diet (%)	Aldrin Consumed (mg/k)		Mortality (%)
					daily	total	
Quail	10	1	6	0.002	0.62	3.3	100
"	40	1	13	.001	1.21	5.7	100
"	17	16	37	.0005	.32	11.1	100
"	10	1	47	.0001	.08	5.6	100
"	32	15	70	.0001	.07	5.8	68.8
"	20	1	14	.0001	.11	1.5	60
Pheasant	20	1	46	.0005	.58	27.2	100
Quail Control	200	1	120	—	—	—	28.5
Pheasant "	200	1	120	—	—	—	31.5

c) Effect of aldrin on reproduction in quail:

Birds	% Aldrin in Diet	Eggs/Hen/Day	% Fertile	% Hatch	% Chicks Surviving		
					1 wk	3 wk	12 wk
Experimental	0.001	0.08	85.7	83.3	100	80	76
Control	0	.53	88.6	82.3	90	87.5	78.3

d) Toxicity of aldrin for young Quail; intermittent feeding; 28 day interval between tests:

Birds	Aldrin (%)	Initial Feeding				Second Feeding			
		Duration (days)	Consumed (mg/k)		Mortality (%)	Duration (days)	Consumed (mg/k)		Mortality (%)
			daily	total			daily	total	
Experimental	0.001	14	0.105	1.47	58.8	7	0.016	0.86	100
Control	0	7	—	—	4.0	-	—	—	—
"	0	14	—	—	4.0	-	—	—	—
"	0	42	—	—	22.0	-	—	—	—

e) Effect of aldrin on growth and survival of young Quail:

Test Weeks	Controls		Aldrin in Diet: 0.0001 %	
	Survival (%)	Weight (g)	Survival (%)	Weight (g)
1	96	16	94	12
2	96	26	94	23
3	96	50	94	38
4	90	70	94	51
5	82	90	94	70
6	78	110	94	94
7	78	124	94	105
8	78	130	0	—
9	78	153	—	—
10	78	163	—	—

f) Effect of aldrin fed to Quail in winter maintenance diet: 781

Birds	Aldrin in Diet (ppm)	Duration (days)	Mortality (%)	Aldrin Consumed (mg/k)	
				daily	total
Experimental	1.0	101	100	0.09	9.1
"	.5	127	97.5	.04	5.1
Control	0	162	8.7	0	0

g) Effect of aldrin fed to Quail, Pheasant during growth: 781

Birds	Aldrin in Diet (ppm)	Duration (days)	Mortality (%)	Aldrin Consumed (mg/k)	
				daily	total
Quail	50	6	100	1.4	8.4
"	20	8	100	1.2	9.6
"	10	13	100	.9	11.1
"	5	28	100	.6	15.4
"	1	42	100	.2	7.1
"	1	47	100	.1	9.0
Quail Control	0	120	24	0	0
Pheasant	20	5	100	1.8	9.0
"	5	46	100	.7	31.3
Pheasant control	0	103	28	0	0

h) Effect of aldrin on reproduction in Quail, Pheasant: 781

Bird	Aldrin in Diet (ppm)		Mortality (%)	Eggs/Hen (average)	Fertile (%)	Hatch (%)	Surviving (%)	
	winter	reproduction					2 wk	6 wk
Quail	0.5	0	25	61	79.4	67	100	77.8
"	.5	.5	100	—	—	—	—	—
"	0	1.0	25	40	91	87.3	92.5	77.8
Quail control	0	0	6.25	52	89	83.9	88.9	83.3
Pheasant	0	10	100	8	85.7	30	62.5	62.5
"	0	2	40	35	66.7	39.1	53.3	46.7
"	0	1	20	40	86	55.6	95.5	81.8
Pheasant control	0	0	0	48	86.6	57.4	94.8	89.7

i) Toxicity of aldrin and other compounds for Bobwhite Quail and Mourning Dove compared; given orally in gelatin capsules: 679

Compound	Quail				Dove			
	LD_{50} (mg/k)	MLD (mg/k)	Av. Wgt Loss (%)	Av. Life (days)	LD_{50} (mg/k)	MLD (mg/k)	Av. Wgt Loss (%)	Av. Life (days)
Aldrin	4.0- 4.5	4	15	3	15-17	12.5	18	4.5
Dieldrin	12.0-14.0	10	20	4	44-46	40	15	3
Toxaphene	80.0-100.0	40	25	3	200-250	100	22	3
Lindane ♂	120.0-130.0	120	25	3	♂♀ 350-400	200	10	2.5
Lindane ♀	190.0-210.0		25	3				

9) Pharmacological, pharmacodynamic, physiological, etc.:

a) Aldrin, by any route of entry, is a central nervous system stimulant producing hyper-irritability, convulsions and/or coma. 2812

b) Nausea, vomiting are usual signs but may not follow very large and rapidly absorbed doses. 2812

c) In mammals, increased reflex excitability, convulsions, bradycardia, vasodepression, miosis have been noted as a consequence of CNS stimulation. 1238 2231,1237

(1) Apparent potentiation of acetylcholine action on heart, intestine occurs.
(2) No evidence exists of a direct effect on choline esterase.
(3) Parasympathetic effects are antagonized partly by atropine and barbiturates.
(4) There is increased sensitivity of spinal centers to acetylcholine without any effect on isolated tissues.
(5) Parasympathomimetic by central stimulation of vagal centers rather than by peripheral stimulation.

d) Aldrin induces liver enlargement, hypertrophy, cloudy swelling and volume increase in hepatic cells. 2221,75

e) Aldrin accumulates and is stored in body fat. 2571

(1) Cattle, fed diets with 25 ppm aldrin, showed 49 ppm in fat after 28 days, 78 ppm after 56 days.
(2) Sheep, fed diets with 25 ppm aldrin, showed 60 ppm in fat after 28 days, 78 ppm on the 56th day.
(3) Fed aldrin at 10 ppm, cattle, sheep showed in fat on 112th day respectively 49 and 55 ppm aldrin.

10) Phytotoxicity:

a) Aldrin is non-phytotoxic, non-systemic; does not, when properly formulated and applied, damage plants. Solvents may, under some conditions, for example addition of summer or dormant oils to aldrin-xylene concentrates, injure plants by reducing the rate of xylene evaporation. 2812 2120 129

b) Does not affect soil microorganisms even in excessive doses. 129

c) At 100 lbs/acre no injury or inhibition of growth in field crops occurred. 1635
d) More toxic, pound for pound, to crop plants than DDT, chlordane, toxaphene; less toxic than BHC, lindane. 294

11) Hazard to wild life:

a) Aldrin is hazardous to fish in ponds and lakes. 828
b) Extremely hazardous to honeybees when used on blooming plants. 3099
c) A hazard to wild birds is suggested by the experiments on Quail and Pheasant quoted above. 780,781

12) Toxicity for insects:

a) Aldrin is a general insect poison, active as a contact and stomach toxicant. It yields neurotoxic symptoms only after a latent period. 353 2812
b) Quantitative:

Insect*	Route	Dose	Dosage	Remarks	
Apis mellifera	or	LD$_{50}$	0.25 μg/insect		910
Blabera fusca	inj	MLD$<$7 da	1.3 μg/g	In acetone-triton.	1986
Blabera fusca	inj	MTD†	2.6 μg/g	In acetone-triton.	1986
Blattella germanica ♀					
chlordane-S strain	inj	LD$_{50}$	26.46 μg/g		431
" " "	inj	LD$_{90}$	70.06 μg/g		431
chlordane-R strain**	inj	LD$_{50}$	127.61 μg/g	$\frac{\text{LD}_{50}\text{ chlordane-R}}{\text{LD}_{50}\text{ chlordane-S}} = 4.82$***	431
" " "	inj	LD$_{90}$	1113.6 μg/g	$\frac{\text{LD}_{90}\text{ chlordane-R}}{\text{LD}_{90}\text{ chlordane-S}} = 15.89$***	431
Chrysops discalis	topical	LD$_{50}$	0.04 mg/fly	Estimated LD$_{50}$.	2707
Chrysops discalis	topical	LD$_{90}$	0.17 mg/fly		
Melanoplus differentialis	topical	LD$_{50}$	1.8 μg/g	In dioxane, acetone, ethanol.	3266,3267
Melanoplus differentialis	or	LD$_{50}$	2.3 μg/g	Fed as deposit on leaves.	3266,3267
Melolontha melolontha	contact	LD$_{50}$ 5 da	2.7 μg/insect	Rel.Tox. 25 BHC tech = 1.	3184
Melolontha melolontha	contact	LD$_{50}$ 5 da	$>$6 μg/insect	" " $<$.4 " " "	3184
Musca domestica	topical	LD$_{50}$	1.6, 1.7 μg/g		
Musca domestica	contact spray	LC$_{50}$ 24 hr	0.056 mg/cc	Turntable, Peet-Grady, no KD$_{10}$ min at LC$_{50}$ 24 hr.	2033 2692
Musca domestica	topical	LD$_{50}$	0.032 μg/fly		
Musca domestica DDT-S	contact	LD$_{50}$ 24 hr	0.044 μg/fly		371
Musca domestica Bell flower	contact	LD$_{50}$ 24 hr	0.076 μg/fly		371
Musca domestica Pollard	contact	LD$_{50}$ 24 hr	0.78 μg/fly		371
Musca domestica (larva, 3 Instar)	or	LC$_{50}$	430 ppm	Aldrin mixed in medium.	666
Oncopeltus fasciatus	topical	LD$_{50}$	10.3 μg/g		2231
Oncopeltus fasciatus ♀	inj	LD$_{50}$ 24 hr	4.5 μg/g	6.9 x as toxic as DDT.	348
Oncopeltus fasciatus ♀	inj	LD$_{50}$ 48 hr	2.5 μg/g	4.6 x " " " "	348
Oncopeltus fasciatus ♀	inj	LD$_{95}$ 24 hr	72 μg/g	14.5 x " " " "	348
Oncopeltus fasciatus ♀	inj	LD$_{95}$ 48 hr	43 μg/g	10.2 x " " " "	348
Protoparce sexta (5 Instar)	topical	LD$_{50}$	487 μg/insect	av. wgt 5.4 (4.7-7.5)g.	1306
Protoparce sexta (5 Instar)	topical	LD$_{90}$	1359 μg/insect	" " " " " "	1306
Periplaneta americana	topical	LD$_{50}$	1.0 μg/g		1757
Aëdes dorsalis (larva)	medium	LC$_{100}$ 24 hr	1 ppm		2282
Aëdes dorsalis (pupa)	medium	LC$_{75}$ 24 hr	1 ppm		2282
Anopheles quadrimaculatus (larva)	medium		0.025 ppm	Lowest conc. for 100% kill.	2020
Anopheles quadrimaculatus (larva)	medium	ca LC$_{98}$	0.01 ppm		2020
Rhagoletis completa	topical	LD$_{50}$	0.06 μg/fly		2692
Dacus dorsalis	topical	LD$_{50}$	0.015 μg/fly		2692

*Adult unless otherwise noted.
**Corpus Christi strain.
***Degree of resistance.
†Maximum tolerated dose.

c) Toxicity measured as pounds of aldrin per acre:

Anthonomus grandis	LD$_{50}$	1.1 lbs/acre	contact and stomach action on dusted food plant.	2276
Anthonomus grandis	LD$_{50}$	2.7 lbs/acre	contact action; insect dusted.	2276
Sphenarium purpurascens:	Field tests on corn, 0.35 lb/acre as a 1.0% dust showed 77.8 (69-88)% kill after 12 hrs, 97.8 (95-100)% kill after 24 hrs. Field tests on corn, 0.82 lb/acre as a 2.5% dust showed 88.6 (83-96)% kill after 12 hrs, 99.6 (99-100)% kill after 24 hrs.			307

Melanoplus differentialis (1st, 2nd Instar) LD_{50} 0.04 lb/acre as contact emulsion sprays made from miscible oil concentrates. In field tests 2 oz/acre, as sprays, give control comparable to chlordane, toxaphene at much higher rates. 0.3 lb/acre as dusts gave complete control, comparable to chlordane, toxaphene at 1 lb/acre. 1102

d) Comparative fumigant action of aldrin and other compounds on adult *Anthonomus grandis*: 2276

Compound	LC_{50} (mg/l)
Aldrin	12.9
Dieldrin	16.6
Chlordane	21.9
BHC (tech)	47.6, 59.2
α-BHC	467.3
β-BHC	1213.0
δ-BHC	778.2
γ-BHC	233.5

e) Toxicity of vapors, aldrin and some other chlorinated hydrocarbons vs. various insecticide resistant and non-resistant biotypes of *Musca domestica*. Toxicity measured as LT_{50} or time in minutes for 50% kills with vapors at saturation in air. 3320

Strain	LT_{50} (minutes)			
	Aldrin	Chlordane	Lindane	Dieldrin
Non-R*	< 15	33	25	40
Orlando #1**	23	69	58	110
LDD***	158	347	173	550
Ballard****	96	380	316	550

*A laboratory maintained strain without appreciable insecticide resistance.

**A strain exposed only to DDT, for which high tolerance developed, with some cross tolerance for lindane, chlordane, dieldrin.

**Strain isolated from a "population" of flies uncontrolled under dairy conditions by DDT, lindane, dieldrin, in which resistance was maintained by constant exposure in cages to insecticide residues.

**A wild strain from a dairy treated, with relative lack of effect, with space and residual lindane applications.

f) Comparative toxicities of aldrin and some other chlorinated hydrocarbons incorporated in a rearing medium for *Musca domestica* larvae. Effect measured as % of adult emergence in exposed as compared with control subjects: 666

Compound	LC_{50} (ppm)	0.95 Fiducial Limits (ppm)
Aldrin	430	340- 595*
Dieldrin	450	355- 595*
Endrin	125	100- 160
Chlordane	1450	1100-1900
DDT	2300	1600-3300

*No statistically significant difference in toxicity between aldrin and dieldrin in these experiences.

g) Aldrin, 1%, in insecticidal baits with sugar or molasses base for fly control. *Musca domestica* adults used as test insect. 1915

Laboratory Tests % Knocked Down Or Dead In			Field Tests Degree Of Control After 24 Hrs
30 min	60 min	24 hrs	
20	76	100	No effective control.

h) Aldrin toxicity for grasshoppers fed on cabbage leaves sprayed in the field 1, 3, 5 days before use with 4 oz aldrin/48 U.S. gallons. 2281

Insect	Days after Spraying	Aldrin % Kill		Dieldrin (2 oz/48 gals) % Kill	
		24 hrs	48 hrs	24 hrs	48 hrs
Camnula pellucida	1	73.9	100	96	100
	3	84	100	78.3	95.4
	5	83.4	100	95.5	100
Melanoplus bivittatus	1	45.8	86.5	87.5	100
	3	40	100	64	100
	5	31.8	96	67.9	100
Melanoplus mexicanus	1	52.2	78.3	82.7	100
	3	.1	79.2	61.5	96
	5	15.4	85.4	96.3	100

i) Aldrin toxicity for adult Anasa tristis by topical application in acetone solution. Kill measured at 72 hrs. 3376

Dosage (µg/g)	Kill (%)
64	93.3
128	100
256	100
512	100

(1) Only parathion and lindane gave superior results.

(2) Kills after 30 min. exposure on surfaces treated 7 days before test with insecticide at 100 mg/ft^2: 0 for 24, 48, 72, and 96 hrs. Dieldrin, parathion, lindane, heptachlor gave superior results in that order. Dieldrin only yielded 100% kill 96 hrs. after exposure.

j) Aldrin toxicity in laboratory tests vs. Aëdes dorsalis, Aëdes vexans: 2283
Kills measured at end of 24 hrs. exposure in distilled water with added aldrin at 75°F.

Stage	Concentration	Mortality (%)
Larva	1 ppm	100
Larva	1 part in 2 millions	96.9
Larva	1 part in 10 millions	95
Pupa	1 part in 2 millions	30.4
Pupa	1 part in 5 millions	34

k) Toxicity of aldrin in sprays for 3rd instar Leptinotarsa decemlineata: 1986
Sprayed at 10g/100 l, 76g/hectare 88% survival at 24, 72% at 48 hrs.
Sprayed at 20g/100 l, 136g/hectare 32% survival at 24, 22% at 48 hrs.

l) Aldrin toxicity for adult Sitophilus granarius in contact with residues on filter paper treated with aldrin in acetone 48 hrs. before exposure of the insects: 1986

Concentration (%)	Survival (%)
0.5	0
.05	0
.005	100

(1) On paper treated 6 months before exposure of the insects:

Concentration (%)	Survival (%)
0.5	44
.05	96

m) Aldrin vs. Prodenia litura, the most injurious pest of cotton in Egypt: 930

(1) As 2.5%, 5% dust on plants bearing eggs of Prodenia, aldrin yielded 100% mortality of all new hatched larvae in 18 hrs. and of larvae of all ages in 24 hrs.

(2) Used alone, aldrin, by destruction of beneficial predators, has led to high increase of red spider and aphid infestations. The disadvantage has been overcome by applying aldrin in a dust at 2.5% with parathion at 1%. The combination yielded 100% kills of eggs and hatched larvae of Prodenia.

(3) The action against larvae of 2.5% dusts of dieldrin is slower, but 100% kill is achieved.

13) Speed of toxic action of aldrin and other compounds vs. Macrosiphum pisi on young Vicia faba plants. Insecticides applied as talc base dusts by the dusting tower method: 520

Compound	Concentration (%)	Temperature (°F)	50% Kill at		98% Kill at	
			hr	min	hr	min
Talc (control)	—	67-72	13	28	23	51
Toxaphene	5	72	13	20	19	1
Chlordane	5	72	9	24	18	8
EPN®	.86	74	5	26	8	6
Dieldrin	1	75	4	7	6	43
Aldrin	1	75	3	44	7	32
DDD	5	72	2	34	4	35
Methoxychlor	10	75	2	1	5	34
Parathion	1	70	1	8	1	43
Parathion	2	70	1	21	1	53
DDT	5	72	0	57	1	45
Lindane	1	72	0	56	1	54
Rotenone*	5	72	0	47	1	23
TEPP**	.18	74	0	20	0	56
Nicotine	1	72	0	15	1	12
Nicotine	3	72	0	12	0	50

*Rotenone 5%, other extractives 10%.
**Tetraethyl pyrophosphate.

14) Toxicity of aldrin and other compounds compared:

a) Vs. Cirphis unipuncta larvae.* 3268

Compound	As Topical Poison		As Stomach Poison		$\frac{LD_{99}}{LD_{50}}$	
	LD$_{50}$ (μg/g)	Ratio to Parathion	LD$_{50}$ (μg/g)	Ratio to Parathion	Topical	Stomach
Aldrin	19.8	5.4	11.4	4.6	3.7	24.7
Parathion	3.7	1.0	2.5	1.0	3.4	8.5
DDT	193	52.2	45.7	18.3	4.7	22.8
Chlordane	117.5	31.6	78.2	31.3	4.9	4.7
Toxaphene	56.2	15.2	34.1	13.6	4.7	2.9
Lindane	28.1	7.6	27.9	11.2	3.2	5.1
Dilan	8.8	2.4	11.5	4.6	5.4	5.0
Dieldrin	8.3	2.2	4.6	1.8	3.1	3.8

*The fastest kill was given by parathion, followed in order by Dilan, lindane, DDT.

b) Vs. Anasa tristis in laboratory tests. Topical application of toxicants in acetone solution to adult Anasa: 3376

Compound	% Kill in 72 hrs at					Action Rate at Least Topical Dose Yielding 90% or > Kill in 72 hrs				
	32μg/g	64μg/g	128μg/g	256μg/g	512μg/g	μg/g	12 hrs	24 hrs	48 hrs	72 hrs
							% Kill			
Parathion	100	100	100	100	100	6	3.3	33.3	76.7	90
Lindane	83.3	100	100	100	100	64	—	80	100	100
Aldrin	—	93.3	100	100	100	64	—	23.3	76.7	93.3
Endrin	—	—	100	100	100	128	6.7	20	80.7	100
EPN®	—	—	100	100	100	128	10	26.7	76.7	100
Heptachlor	—	83.3	90	100	100	128	10	50	80	90
Isodrin	—	—	90	100	100	128	0	10	63.3	90
Dieldrin	—	—	70	100	100	256	0	70	96.7	100
Chlordane	—	—	36.7	80	90	512	—	6.7	73.3	90
Toxaphene	—	—	16.7	66.7	82	—	—	—	—	—
DDT	—	—	20	30	76.7	—	—	—	—	—

Adult Anasa mortality after 30 min exposure to surfaces insecticide treated 7 days before at 100 mg/ft^2:

Compound	% Kill in			
	24 hrs	48 hrs	72 hrs	96 hrs
Dieldrin	30	80	80	100
Parathion	10	10	20	40
Lindane	10	20	20	20
Heptachlor	0	10	20	20
Aldrin	0	0	0	0

c) Comparative toxicity vs. Apis mellifera; various routes of application and exposure: 1718

	Oral Dose, μg/Bee, to Yield % Kill Shown in 24 hrs			Contact Spray Dose, μg/cm^2, to Yield % Kill Indicated			Effect of 1 hr Contact With Residual Dry Films				Effect of Residual Film Vapors 1 hr Exposures	
	20%	50%	90%	20%	50%	90%	% Kill 24 hrs	μg/cm^2	Field Av. Dose μg/cm^2	oz/acre	% Kill 24 hrs	μg/cm^2 Dry Film
Parathion	0.018	0.04	0.144	0.257	0.354	0.574	90	0.54	1.4	2	100	5.0
							10	.18			0	2.8
TEPP	.052	.065	.093	.358	.445	.621	8	.22	5.6	8	0	5.5
Lindane	.026	.079	.346	.772	.851	.986	100	.28	2.8	4	100	.44
							0	.074			0	.28
Dieldrin	.223	.269	.354	.386	.572	1.052	90	.09	1.4	2	100	.28
							10	.04			0	.074
Aldrin	.181	.239	.365	.327	.562	1.274	75	.09	1.4	2	100	.74
							0	.04			0	.074
Chlordane	.831	1.122	1.730	3.802	5.0	7.58	100	3.4	11.2	16	100	3.7
							12	.90			0	.37
Systox®	1.256	1.478	1.884	4.321	5.123	6.619	50	10.0	—	—	0	18.5
							22	6.8				
Dimefox®	1.25	1.905	3.506	16.52	23.17	38.64	0	50.0	—	—	0	74.0
Toxaphene	25.12	39.81	80.17	36.73	44.67	59.92	9	110.0	16.8	24	0	70.0
							0	40.0				

15) Mode of action and other effects in insects:

a) Physiological effects: Superficially DDT-like; neurotoxic symptoms follow a pronounced latent period. As with DDT, hyperexcitability, agitation are succeeded by inability to coordinate movements, paralysis and death. 2231 353

- (1) Elicits repetitive discharge (action potential) in Periplaneta nerve. 1901
- (2) 10 μg, by injection in Blattella germanica; after a 2-3 hour latent period, induced a sharp, rapid rise in oxygen consumption (from 0.5 to ca 3 mm^3/min/insect). The peak of respiration was reached ca. 5 hours after injection. Insect remained passive during latent period. 1441
- (3) The temperature coefficient of toxic action (in contrast to DDT) is positive. Greater mortality of Musca, exposed continuously to residual deposits, occurred at 90°F than at 70°F. The reverse was true for DDT, DDD, methoxychlor. 1561
- (4) More toxic for Blattella held at high post-treatment temperatures than at lower temperatures. This is in contrast to DDT, lindane, pyrethrins. 1305

b) Biochemical conversion of aldrin to dieldrin in the insect and mammalian body is suggested. 2231
  - (1) Dehydrochlorination is not, apparently, the toxic mechanism.

16) Fate of aldrin and dieldrin in the animal body. Recent experiences by Bann, J. M., et al., Journal of Agricultural and Food Chemistry 4 (11): 937, 1956.*
  - (1) In beef and dairy cattle, pigs, sheep, rats, poultry and presumably in all animals, aldrin undergoes ready, rapid and fairly complete epoxidation to dieldrin.
  - (2) The above appears to be independent of the site of aldrin entry as it follows intake by the oral and the subcutaneous route.
  - (3) The dieldrin thus formed (and presumably dieldrin taken into the body as such) is stable and is stored unchanged in the body, being recoverable from milk, butter, cream, eggs and tissue fat.

EXPERIENCES IN THE CONTROL OF INSECTS OF ECONOMIC IMPORTANCE IN THE FIELD USING ALDRIN

a) Suggestions of the manufacturer: 2812
  - (1) As emulsible concentrate 0.07-0.25 lb aldrin/acre effective vs. boll weevil, cotton leafworm, tarnished plant bug, southern green stinkbug, grasshoppers, fall armyworm, rapid plantbug, cutworms (certain species), thrips (certain species), loopers (certain species).
  - (2) As a wettable powder, 0.25 lb aldrin/lb, effective vs. wireworms of tobacco, tomatoes, potatoes, sweet potatoes, sugar cane, corn, sugar beets, and small grains at 12 lbs/acre; white grubs of sugar cane at 20 lbs/acre, of beets, corn, grains at 12 lbs/acre; sugar beet maggots at 12 lbs/acre; peanut rootworms at 8 lbs/acre; corn rootworms at 4 lbs/acre; Anomala beetle of pineapple at 10-20 lbs/acre before planting.
  - (3) As aldrin granules, aldrin 2%, vs. Japanese beetle grubs, European chafer grubs, white grubs, June beetle larvae, lawn chinch bugs, turf ants at 150 lbs aldrin/acre, 1 lb/300-400 ft^2.
  - (4) As aldrin-fertilizer mixture, 0.5% aldrin, vs. corn rootworm, at 200 lbs/acre (actual aldrin 0.5-1.0 lb/acre).
  - (5) Effective vs. cotton pests at 4-6 oz/acre, vs. grasshoppers at 2-3 oz/acre, vs. soil pests at 0.5-6 lbs/acre. 2120

b) Other data:
  - (1) Commercial control, Diabrotica longicornis, obtained at 1 lb aldrin/acre on ridge planted corn by 3 procedures, on surface-planted corn by 1 method. 1997
  - (2) Effective in field control of Trombiculid vectors of scrub typhus. 3110
  - (3) Superior to DDT in control of elatrids, scarabeids. 353
  - (4) Gave 98% control, Melanoplus leukinus, over 40,000 acres sprayed at 2 oz aldrin/gallon/acre. 353
  - (5) Outstandingly effective vs. grasshoppers at 2-4 oz/acre. 3266
  - (6) Twice as toxic as chlordane, which is more toxic than DDT, vs. Blissus hirtus in turf. 2776
  - (7) As 2.5% dusts, superior to DDT 10% dusts vs. Thrips tabaci. 3303
  - (8) Effective (but with residue danger) vs. cabbage maggot. 353
  - (9) 10 times as effective as DDT vs. Dacus dorsalis. 483
  - (10) More effective than Parathion vs. Popillia japonica grubs. 2779
  - (11) Equal in 0.025% suspension to DDT in 0.1% suspension vs. Leptinotarsa decemlineata. 2779
  - (12) Effective vs. ants; better than chlordane vs. Lasius niger, L. exsectoides. 2779
  - (13) 5 times as effective as chlordane (tech.) vs. Musca domestica; lacks KD power. 1152
  - (14) Effective vs. Stomoxys species. 921
  - (15) At 0.75 lb/100 gal., 70% direct, 74% residual reduction of Pyrausta nubilalis yielded. 675
  - (16) Ineffective vs. Empoasca. 2280
  - (17) Less effective than DDT vs. corn earworm. 158
  - (18) Compares unfavorably with DDT vs. Simulium larvae. 1549

EFFECTIVENESS DATA FROM SCREENING TESTS

1) Methods of testing to be found in the reference given. 1801
  - a) Vs. adult lice: Effective on cloth for 31 days or more with mortality.
  - b) Vs. louse eggs: 0-50% kills with 5% solutions.
  - c) Vs. body louse: KD action complete in 1 hour on impregnated pads.
  - d) As mosquito larvicide:
    - (1) Vs. Anopheles quadrimaculatus gave 95-100% kills at 0.01 ppm.
    - (2) Vs. Aëdes aegypti, Culex quinquefasciatus gave 50-100% kills at 1 ppm.

---

*Attention was drawn to this paper too late to permit its inclusion in the alphabetic, cumulative bibliography of this work.

e) As a space and residual spray vs. flies, mosquitoes:
   (1) Space spray vs. flies gave 50% or more kills with 1% solution.
   (2) " " vs. *Aëdes aegypti* gave 10-49% kills with 2% solution.
   (3) Residual vs. flies, *Aëdes aegypti* gave 90-100% kills after 1 week but less than 100% kills after 4 weeks.

f) As dusts vs. *Blattella germanica* gave 91-100% kills after 48 hours with similar results as a residue treatment.

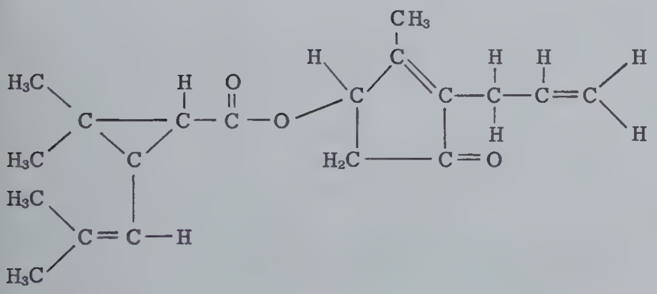
g) Vs. fleas:
   (1) As dust vs. *Ctenocephalides felis* effective for > 10 days.
   (2) Insecticidally ineffective on initial test, fleas not all down in 1 hour.
   (3) Vs. *Xenopsylla cheopis*, ineffective in 1 hour insecticidal and "KD" tests; as dusts effective for > 10 days.

h) Vs. chiggers, ticks:
   (1) In insecticidal and "KD" tests, ineffective for ticks (not all down within 15 minutes).
   (2) In insecticidal and "KD" tests vs. chiggers all "knocked down" in 15 minutes; insecticidally effective on initial test but ineffective after a 15 minute rinse.

i) Repellency:
   (1) Ineffective after 1 day as flea and tick repellent on cloth.

3

ALLETHRIN (DL-2-Allyl-3-methylcyclopent-2-en-4-ol-1-onyl DL-cis-trans-chrysanthemate; DL-Allylrethronyl DL-cis-trans-chrysanthemate; DL-2-Allyl-4-hydroxy-3-methyl-2-cyclopenten-1-one ester of cis-trans-DL-chrysanthemum monocarboxylic acid.)



Molecular weight 302.4

GENERAL

A synthetic pyrethroid having insecticidal powers and properties similar to those of the naturally occurring 2752
pyrethrins and other synthetics such as cyclethrin and furethrin, q.v. 2231

PHYSICAL, CHEMICAL

The commercial product is a clear, pale, yellow to brownish, viscous liquid containing 75%-95% allethrin 2231
isomers. A crystalline substance, α-DL-trans-allethrin, may be isolated from technical allethrin; m.p. 2221
(crystalline isolate) 50.5°-51°C; b.p. (technical) ca 160°C; $d_{20°}$ 1.005-1.015; $n_D^{20°}$ 1.5040; insoluble in H_2O; soluble 2753
in most organic solvents; miscible in petroleum oils; soluble in alcohol, carbon tetrachloride, petroleum ether, 252
ethylene dichloride, nitromethane; incompatible with alkalis; chemical properties similar to those of the natural 1248
pyrethrins, but allethrin is more stable on exposure to heat and ultra-violet rays; detoxified by double-bond 1891
hydrogenation of the acid or allyl side chains; may hydrolyze to yield chrysanthemic acid and 2-allyl-3-methyl-2, 2667
4-cyclopentadienone which dimerizes by the Diels- Alder reaction; compatible with sulfur in dust formulations. Allylrethrolone and chrysanthemic acid, the two constituents of allethrin, exist as optical isomers. Chrysanthemic acid is stereo-isomeric. Thus, there are 8 optical and geometric isomers of allethrin, all potentially present in the technical product, whose insecticidal activity depends on the proportions in which the isomers are present.

The isomers are:
D- and L- Allylrethronyl D- cis-chrysanthemate
D- and L- Allylrethronyl L- cis-chrysanthemate
D- and L- Allylrethronyl D- trans-chrysanthemate.
D- and L- Allylrethronyl L- trans-chrysanthemate

1) Formulations: In odorless kerosene; as aerosols; as impregnated dusts.
2) Allethrin synergizes insecticidally with the usual pyrethrin synergists: Piperonyl butoxide, q.v., n-propyl isome, q.v., piperonyl cyclonene, q.v., n-octyl sulfoxide of isosafrole, q.v., etc. Also consult the general treatment titled, Synergists, Synergism.
   a) N- (2-ethylhexyl) imide of endomethylenetetrahydrophthalic acid, or Van Dyke 264, q.v., also synergizes effectively with allethrin.

TOXICOLOGICAL

1) Allethrin toxicity is comparable, in general, to the toxicity of natural pyrethrins. Kidney and liver damage 2231
follow the entry, by any route, of toxic dosages. Lung congestion may also ensue. 2221

2) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	480	In kerosene; 20% commercial sol.	478
Rat	or	LD_{50}	920	In kerosene; 20% commercial sol.	478
Rat	or	LD_{50} ca	680		1951
Rabbit	or	LD_{50}	4290	In kerosene; 20% commercial sol.	478
Rabbit	ct	LD_{50}	11.2 cc/k	Single, acute inunction.	478

   a) Administered to rats by inhalation in dosages 10,000 times as great as those normally used in fly-killing 2231
   aerosols, in single exposure and to ten times the amounts normally used, in multiple exposures 90% of the 356
   exposed subjects survived.
   b) Applied to shaved rabbits by means of impregnated cloth, allethrin produced a transient erythema. 356

3) Chronic toxicity for higher animals:
   a) Rats have tolerated allethrin in the diet at 2000 ppm for about 1 year without overt effects or histopathological signs. 356
   b) Rats tolerated, without overt effects, for 16 weeks a diet with 5000 ppm allethrin. 1953
   c) The lability of allethrin virtually excludes any serious residue hazard.

4) Pharmacological, pharmacodynamic, symptomatological, physiological, etc.
   a) The toxicological properties of allethrin resemble those of the natural pyrethrins. The following effects 1953
   may be noted: 536
      (1) Nervous effects resembling veratrine poisoning.
      (2) Tremor, excitation, passing over to convulsions, clonic spasm, muscular fibrillation, incoordination, tetanic muscular paralysis, respiratory failure and death.
      (3) If the intoxication is not fatal, a complete recovery ensues.
      (4) Pentobarbital and ether anesthesias suppress the convulsive stages; atropine controls the concomitant diarrhoea. 1971
   b) Histopathological signs (rats, rabbits): 2231
      (1) Cloudy swelling in cells of kidney tubules.
      (2) Cloudy swelling of hepatic parenchyma cells.
      (3) Free pigment in the liver stroma and in the littoral cells of von Küppfer.

5) Phytotoxicity:
   a) As in the natural pyrethrins, the toxicity for plants is of a low order. Not to be overlooked are the potential phytotoxic effects of such solvents or carriers with which allethrin may be combined. 3324

6) Toxicity for insects:
   a) Quantitative.

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti, 3rd instar	Medium	LC_{50}	0.19 ± .03 S.D. ppm		1248
Anopheles quadrimaculatus, adult 4 days ♂	topical	LD_{50}	0.0029 µg/insect	ER* to DDT = 6.9.	2051
A. quadrimaculatus, adult 4 days ♂	topical	LD_{90}	0.13 µg/insect	ER* to DDT = 3.5.	2051
A. quadrimaculatus, adult 4 days ♀	topical	LD_{50}	0.008 µg/insect	ER* to DDT = 8.3.	2051
A. quadrimaculatus, adult 4 days ♀	topical	LD_{90}	0.041 µg/insect	ER* to DDT = 3.2.	2051
Blattella germanica, adult ♀ DDT-S	topical	LD_{50}	0.76 µg/insect	Synergized.	1012
B. germanica, " " DDT-R	topical	LD_{50}	1.3 µg/insect	Synergized. DR** = 1.7.	1012
B. germanica adult ♀ Chlordane-R	topical	LD_{50}	1.0 µg/insect	Synergized. DR** = 1.3.	1012
B. germanica ♂	topical	LD_{50}	60-66, 47-52 µg/g	Nelson Drop Test.	2291
B. germanica ♀	topical	LD_{50}	58-64, 50-55 µg/g	Nelson Drop Test.	2291
Musca domestica, adult	topical	LD_{50}	0.42 µg/fly	Kill ***24 hrs. post-treatment.	3130

Insect	Route	Dose	Dosage	Remarks	
Musca domestica, adult	topical	LC_{50}	0.35 mg/cc	Kill 24 hrs. post-treatment.	3130
M. domestica, adult	topical	LD_{75}	0.50 μg/fly	Kill 24 hrs. post-treatment.	3130
M. domestica, adult	topical	LC_{75}	0.42 mg/cc	Kill 24 hrs. post-treatment.	3130
M. domestica, adult	contact spray	LC_{50}	0.787 ± .034 mg/cc	Turntable; refined kerosene.	1162
M. domestica, adult	contact spray	LC_{50}	0.782 ± .054 mg/cc	Turntable; refined kerosene.	1162
M. domestica, adult DDT-S	topical	LD_{50} 24 hrs.	0.3 μg/fly	Applied to thorax.	2291
M. domestica, adult, Bellflower DDT-R	topical	LD_{50} 24 hrs.	1.0 μg/fly	Applied to thorax.	2291
Oncopeltus fasciatus	topical	LD_{50}	30-40, 25-35 μg/g	Nelson Drop Test.	2291

*ER = Effectiveness Relative.
**DR = Degree of Resistance.
***Kill = Mortality.

b) Comparative toxicity.

(1) As water emulsion sprays: 2291

Insect	Pyrethrins mg/100cc	Kill %	Allethrin mg/100cc	Kill %
Oncopeltus	6.5	42	6.5	12
"	6.5	50	6.5	14
Pieris rapae	3.3	75	3.3	48
" "	3.3	67	3.3	50
" "	6.5	29	13	42
Heliothis (3rd instar)	6.5	70	6.5	50
" (5th ")	13	66	13	38

(2) As impregnated dusts. 2291

Insect	Pyrethrins (%)	Kill (%)	Allethrin (%)	Kill (%)
Oncopeltus	0.23	46	0.46	21
" (larva)	.23	50	.46	17
Pieris rapae	.23	52	.46	39
Cabbage Looper	.23	54	.46	30

(3) Allethrin samples from various makers compared with pyrethrins vs. Musca domestica by the Peet-Grady Test: 2291

Pyrethrins g	KD 10 min* %	Kill 24 hrs %	Allethrin g	KD 10 min** %	Kill 24 hrs %
0.012	95	—	0.012	95	—
.012	94	48	.012	80	11
.012	99	34	.012	98	43
.012	71	14	.012	74	23
.008	70	12	.012	59	6
—	—	—	.004	70	12

*KD 5 min = 90%.
**KD 5 min = 70%.

(4) Allethrin and pyrethrins compared vs. nymphs of Periplaneta americana (= P) and Blatta orientalis (= B) by direct spray method; 12 cc dose, sprays of pyrethrin or allethrin, 0.1 g/100 cc: 2291

Substance	KD % 5 min		KD % 10 min		KD % 30 min		Kill % 24 hrs		Kill % 48 hrs		Kill % 72 hrs		Kill % 144 hrs	
	P	B	P	B	P	B	P	B	P	B	P	B	P	B
Pyrethrins	2	7	3	18	55	55	48	39	52	40	52	45	57	62
Allethrin	0	0	0	0	3	13	5	5	3	7	5	12	7	20
Control							0	3	0	11	0	13	2	18

(5) LD_{50}, by topical administration, allethrin, pyrethrins, DDT, for 3 insect species: 2291

Insect	Allethrin	Pyrethrins	DDT	Remarks
Musca domestica Lab DDT-S	0.3 μg/fly*	1.0 μg/fly*	0.03 μg/fly*	Applied to thorax.
Musca domestica Bellflower DDT-R	1.0 μg/fly*	1.0 μg/fly*	11.0 μg/fly*	Applied to thorax.
Blattella germanica ♂	60-66; 47-52 μg/g	10-15 μg/g	—	Nelson Drop Test.
Blattella germanica ♀	58-64; 50-55 μg/g	10-15 μg/g	—	Nelson Drop Test.
Oncopeltus fasciatus	30-40; 25-35 μg/g	4-5 μg/g	—	Nelson Drop Test.

*LD_{50} 24 hrs.

(6) Toxicity, evaluated by the Turntable Method, of allethrin, allethrin analogues, pyrethrins as sprays in refined kerosene, vs. Musca domestica: 1162

Compound	LC$_{50}$, mg/cc	Relative Toxicity
Allethrin methyl analogue	6.47 ± 0.49	0.4 ± 0.03 0.12xs as toxic as allethrin.
Allethrin ethyl analogue	2.99 ± .44	.94 ± .14 0.26xs " " " "
Allethrin	.787 ± .034	3.29 ± .18 xs as toxic as pyrethrins.
Allethrin	.782 ± .054	3.61 ± .27 xs " " " " "
Pyrethrins	2.593 ± .09	1.0 (standard)
Pyrethrins	2.825 ± .08	1.0 (standard)

a) Data for other allethrin analogues may be found by consulting References 1159, 1643.

c) Allethrin and synergists:

(1) Toxicity of allethrin and allethrin + synergist vs. Musca domestica; topical application; mortality 24 hrs after treatment: 3130

Insecticide	Dose	Dosage	Relative Toxicity
Allethrin	LD$_{50}$	0.42 µg/fly	
"	LC$_{50}$	.35 mg/cc	
"	LD$_{75}$	.50 µg/fly	1.0
"	LC$_{75}$	.42 mg/cc	
Allethrin + piperonyl butoxide, 1:1	LD$_{75}$	.17 µg/fly	2.47
" " " " "	LC$_{75}$	.2 mg/cc	
" + n-propyl isome, 1:1	LD$_{75}$	.19 µg/fly	2.21
" " " " " "	LC$_{75}$	.23 mg/cc	
" + Araclor 5460	LD$_{75}$	.33 µg/fly	1.27
" " " "	LC$_{75}$	.39 mg/cc	
" " " "	LD$_{50}$	.31 µg/fly	
" " " "	LC$_{50}$	.26 mg/cc	

(2) Vs. Aëdes aegypti, 3rd instar: 1248

Toxicity

Insecticide	LC$_{50}$ (ppm)
Allethrin	0.19 ± .03 S.D.
Allethrin + Sulfox-cide, 1:5	.17
" " piperonyl butoxide, 1:5	.18
Pyrethrins	.059 ± .02 S.D.
Pyrethrins + Sulfox-cide, 1:5	.04
" + piperonyl butoxide, 1:5	.05

Stability

Compound	LC$_{50}$, ppm			
	Fresh	UV Light 5 hrs	Heat, 3 days 110-120°F	Room 1 week
Allethrin	0.11	0.53	0.22	0.36
Pyrethrins	.05	.65	.60	.59

(3) Stability of allethrin, pyrethrins under various conditions; tested vs. Musca domestica, 5 day old adults: 1248

Compound	Fresh		UV Light, 5 hrs		Heat, 110°-120°F, 3 days		Room, 1 week	
	KD 10 min %	Kill 24 hrs %	KD 10 min %	Kill 24 hrs %	KD 10 min %	Kill 24 hrs %	KD 10 min %	Kill 24 hrs %
Allethrin	97	39	96	19	96	28	95	30
Pyrethrins	91	23	95	19	94	19	100	15

(4) Allethrin and pyrethrins, tested as settling mists in Deobase Oil, vs. Periplaneta americana and Blattella germanica: 1248

Compound	P. americana			B. germanica		
	Conc. %	KD 30 min %	Kill 4 days %	Conc. %	KD 10 min %	Kill 2 days %
Allethrin	1.6	95	85	0.2	79	70
"	1.2	65	40	.1	70	63
"	8	15	10	.05	61	56
"	.4	0	0	—	—	—
Pyrethrins	.4	100	80	.2	100	91
"	.3	100	65	.1	100	70
"	.2	70	35	.05	100	70
Deobase Oil Control	100	0	0	100	0	26

(5) Effectiveness, vs. various insects, of allethrin as sprays and aerosols with comparative data for pyrethrins. Insecticides synergized by n-propyl isome, Van Dyke 264, piperonyl butoxide in low pressure aerosols and by piperonyl butoxide, n-propyl isome, sesame oil and sesame oil fractions in high pressure aerosols. Applied at rate of 4.63 g/1000 ft^3: 961

Substance	Musca domestica				Periplaneta americana	
	% KD in			% Kill	% Mortality in	
	5 min	10 min	15 min	1 day	1 day	5 days
Allethrin aerosol	44	69	82	32	—	—
Pyrethrin aerosol	53	73	81	32	—	—
Allethrin spray	75	87	—	25	0†	12†
" "	—	—	—	—	0††	0††
Pyrethrin spray	76	84	—	25	2†	18†
" "	—	—	—	—	3††	42††
Allethrin aerosol*	72	83	92	52	—	—
" " **	58	71	85	53	—	—

*4 months old.
**Freshly made.

† Large nymphs.
†† Adult ♀ .

Vs. adult mosquitoes, as sprays:

Spray	Dosage	Anopheles quadrimaculatus			Aëdes aegypti		
		KD 10 min	Kill 1 day, %		KD 10 min	Kill 1 day, %	
			♂	♀		♂	♀
Allethrin	9.26 cc/1000 ft^3	High	65	16	—	—	—
Allethrin	55.56 cc/1000 ft^3	All	100	99	All	100	99
Pyrethrins	9.26 cc/1000 ft^3	Medium	73	43	—	—	—
Pyrethrins	55.56 cc/1000 ft^3	High	67	38	High	82	62

Substitution of allethrin in the "Tentative Official Test" vs. Musca domestica: 961

Aerosol Formula	Concentration, %	KD, %			Kill, %
		5 min	10 min	15 min	1 day
Allethrin	0.4				
DDT	2				
Methylated naphthalenes	6	17	36	48	71
Kerosene, odorless	6.6				
Freon 11, Freon 12, 1:1	85				
Pyrethrum, 20% pyrethrins	2				
DDT	2				
Methylate naphthalenes	6	15	28	39	72
Kerosene, odorless	5				
Freon 11, Freon 12, 1:1	85				

Substitution of allethrin in the U.S. Public Health Service aircraft aerosol formulae vs. Musca domestica, Anopheles quadrimaculatus, Aëdes aegypti: 961

Aerosol Formula	Conc., %	M. domestica		Anopheles; Aëdes		
		KD 15 min, %	Kill 1 day, %	KD 15 min, %	Kill 1 day, %	
					♂	♀
Allethrin	1.2					
Methylated naphthalenes	8	98	99.5	100	100	100
DDT	2					
Freon 12	88.8					
Pyrethrum, 20% pyrethrins	6					
Methylated naphthalenes	8	92	98	High	100	100
DDT	2					
Freon 12	84					

In aerosols allethrin did not lose its effectiveness in 15 months of storage when tested vs. Musca. Formulated with DDT in aerosols, there was no loss of effectiveness vs. Musca after 10 months of storage. 962

(6) Allethrin toxicity by contact for Musca biotypes; LD_{50} 24 hrs at 60°F: 371

Biotype		LD_{50}, μg/fly
Laboratory,	DDT-S	0.43
Bellflower,	DDT-R	.97
Pollard,	DDT-R	.50

7) Comparisons of allethrin and natural pyrethrins vs. some insects: 935
a) ± -3Methyl-2-allyl-cyclopent-2-en-4-ol-1-one esterified with:
(1) (+)-Trans-chrysanthemum monocarboxylic acid (natural).
(2) (±)-Cis-trans-chrysanthemum monocarboxylic acids (synthetic)
yielded:
(3) (±)-Allylrethronyl (+) transchrysanthemate.
(4) (±)- Allylrethronyl (±) cis-transchrysanthemate.

b) The esters were compared with pyrethrin I, II stocks containing 3.01% total pyrethrins by application as contact sprays in the Potter tower to test insects. The aqueous medium contained: 0.1% sulfonated Lorol® and 10% acetone. All insects were sprayed on the same occasion under similar conditions as follows:

Insect	Deposit (mg/cm^2)	°C	Humidity (%)	Holding (°C)	Holding Relative Humidity (%)
Plutella maculipennis (last instar)	7.01	23.5	47.5	17	55
Macrosiphum solanifolii (adult ♀, apterous)	6.78	20	61.5	18	60
Phaedon cochleariae (adult)	6.52	19.5	46.5	17	55
Oryzaephilus surinamensis (adult)	6.79	16.5	54	17	55

c) Symbols:

Extract natural pyrethrins - I
+, (±) allylrethronyl (+) transchrysanthemate - II
+, (±) allylrethronyl (±) cistranschrysanthemate - III

(1) Toxicities of I, II, III compared:

Insect	LC$_{50}$ (w/v) % I	LC$_{50}$ (w/v) % II	LC$_{50}$ (w/v) % III	Relative Potency I	Relative Potency II	Relative Potency III
Plutella	.00574	.001415	.003162	1000	3980	1820
Macrosiphum	.00034	.00275	.00589	1000	123	58
Phaedon	.000324	.000813	.001662	1000	399	200
Oryzaephilus	.00537	.01122	.01318	1000	479	406

(2) Maximum variations in absolute toxicity:

Substance	Insect	Minimum LC$_{50}$ w/v % (A)	Insect	Maximum LC$_{50}$ w/v % (B)	$\frac{B}{A}$
I	Phaedon	.000371	Plutella	.00899	ca 24
II	Phaedon	.000662	Oryzaephilus	.0112	ca 17
III	Phaedon	.00201	Oryzaephilus	.0261	ca 13

(3) Comparison of toxicities observed in sprayings on different days:

Insect	LC$_{50}$, w/v, % I	II	III	Difference Significant	Difference Not Significant
Plutella	.00899	.00251		*	
"	.00346		.00241		
Macrosiphum	.00541	.00272		*	
"	.00704	.0092			
Phaedon	.000371	.000662		*	
"	.000305	.00201			
Oryzaephilus	.00552	.0112		*	
"	.00789	.02607			

8) General remarks: Insecticidal properties of allethrin: 1801

a) Screening tests have indicated high activity vs. human body lice both in insecticidal and "knock-down" effect; high activity as a larvicide vs. Aëdes aegypti, Culex quinquefasciatus; good activity as a space and residual spray vs. Musca and as space sprays vs. mosquito adults.

9) Chemical structure and toxicity: Allethrin, allethrin isomers, allethrin analogues:

a) Allethrin isomers vs. Musca domestica 1163

Isomer	Relative Toxicity
DL-Allylrethronyl DL-cis-transchrysanthemate	1.0 (standard)
L- Allylrethronyl D-trans-chrysanthemate	.66
L- Allylrethronyl L-trans-chrysanthemate	.026
D- Allylrethronyl D-trans-chrysanthemate	3.86
D- Allylrethronyl L-trans-chrysanthemate	.16

b) Optical- and stereo-isomerism: Effects on toxicity for insects: 934,935

(1) DL-Allylrethronyl D-chrysanthemate (trans) as a water spray is twice as toxic for Phaedon cochleariae, Plutella maculipennis as DL-Allylrethronyl DL-cis-transchrysanthemate; DL-allylrethronyl DL-trans-chrysanthemate is more than twice as toxic for Phaedon, Plutella as the DL-cis-chrysanthemate.

(2) Topically applied, or injected, the D-trans-chrysanthemate of DL-allylrethrolone is 40 times as toxic as the L-trans-chrysanthemate for Plutella and 50 times more toxic for Dysdercus fasciatus.

(3) The effectiveness ratio varies with the test insect: For Oryzaephilus surinamensis (spray tests) DL-allylrethronyl D-trans-chrysanthemate is 1.2 times as toxic as DL-allylrethronyl DL-cis-trans-chrysanthemate. Vs. Tenebrio molitor (topical application) the toxic ratio of the forementioned isomers is 3.5. Vs. Macrosiphum solanifolii, Plutella maculipennis, Phaedon cochleariae (spray tests) the toxic ratio of the two isomers is 2.

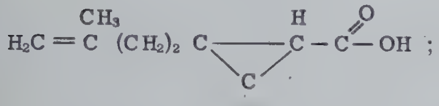
(4)

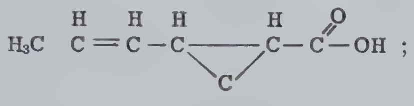
Insect	Relative Toxicities		
	Pyrethrins (standard)	DL-Allylrethronyl-D-transchrysanthemate	DL-Allylrethronyl-DL-cis-transchrysanthemate
Plutella maculipennis	1.0	3.98	1.82
Macrosiphum solanifolii	1.0	.123	.058
Phaedon cochleariae	1.0	.399	.2
Oryzaephilus surinamensis	1.0	.479	.406

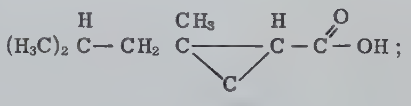
(5) Allethrin vs. *Musca* is equally effective compared with natural pyrethrins, but inferior to natural pyrethrins vs. *Periplaneta*, *Tribolium*, *Oncopeltus* and certain other insects. Vs. *Musca* allethrin may be more toxic than mixed pyrethrins of natural origin, but is said to synergize less well with piperonyl compounds. Vs. *Anopheles quadrimaculatus* (larva) the MLD_{100} is 0.2 ppm and the next lowest concentration yielding 98% kill is 0.1 ppm. 2291 961 2752 353 2020

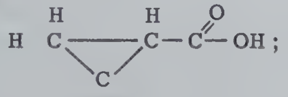
c) Properties of DL-allylrethrolone esterified with carboxylic acids related to chrysanthemic and pyrethric acids; effects vs. *Musca domestica* as sprays in kerosene: 1892

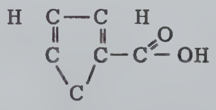
(1) The following acids gave esters with pronounced "knock-down" effect but low killing action:



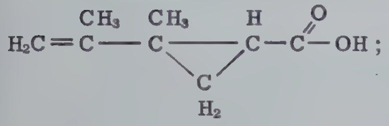


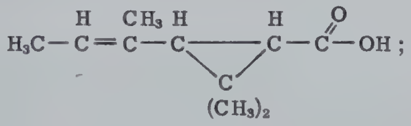


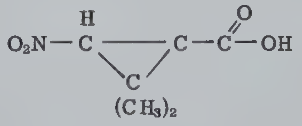




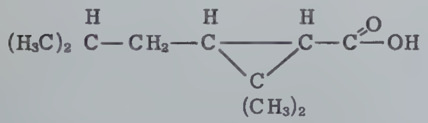
(2) The following acids gave esters with 0.03 times the toxicity of DL-allylrethrolone D-trans-chrysanthemate:







(3) With 0.16 times the toxicity of DL-allylrethronyl D-trans-chrysanthemate:



(4) With 0.05 times the toxicity of DL-allylrethrolone D-trans-chrysanthemate:

d) Changes in the alcoholic (allylrethrolone) component and toxicity:

(1) Side chain modification and effects on *Musca domestica* in spray tests, allethrin standard: 1651

Side Chain	KD Ratio	Mortality Ratio
Methyl	0.44	0.97
Ethyl	.6	.85
n- Propyl	.44	.86
n- Butyl	.39	.8
2- Isobut-2-enyl	.59	.65
2- Isopent-2-enyl	.39	.13

(2) Toxicity comparisons between allethrin analogues, prepared as 2-alkenyl-3-methyl-cyclopent-2-en-4-ol-1-onyl D-trans-chrysanthemates, and natural pyrethrins:

(a) As kerosene spray, allylrethronyl D-transchrysanthemate is 6.6 xs as toxic for *Musca domestica*. 1162

(b) As kerosene spray, methylallylrethronyl D-transchrysanthemate is 3.5 xs as toxic for *Musca*.

(c) As kerosene spray, but-2′ -enylrethronyl D-transchrysanthemate is 1.5xs as toxic for *Musca*.

(d) As aqueous contact spray, allylrethronyl D-transchrysanthemate is 2xs as toxic as methylallylrethronyl D-transchrysanthemate for *Phaedon cochleariae*. 934

(e) As kerosene spray, DL-furfurylrethronyl DL-cis-transchrysanthemate is 0.33 times as toxic for *Musca domestica* as allethrin. 1161

(f) DL-Cyclopentenylrethronyl DL-cis-transchrysanthemate is = to allethrin in toxicity. 1456

e) Miscellaneous structural considerations:

(1) With chlorination of allylrethrolone side chains to give 2′ -and 3′ -Chlorallylrethrolones toxicity declines to ca 0.5 that of corresponding unchlorinated compounds. 1159

(2) Substitution of phenyl for methyl at Carbon 3 in the cyclopentenolone ring, or of allyl for H at Carbon 5 yields decline in effectiveness vs. *Musca* (ca 0.15 the toxicity of allethrin). 1148

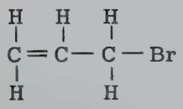
(3) The D-trans-chrysanthemate of 3-hydroxy-8-nonene-2,5-dione, an uncyclized analogue of allethrin is less than 0.09 times as toxic to *Musca domestica* as allethrin, but has good "knock-down" effect. 1148

(4) KD and mortality ratios (Standard, Allethrin) of various chrysanthemic acid esters vs. Musca: 1456

Ester	KD Ratio	Mortality Ratio
Piperonyl	0.38	0.29
Vanillin	.15	.43
Anisic	.18	.56
Guaiacol	.18	.36
Eugenol	.17	.45
Benzyl	.16	.70
Phenyethyl	.13	.42
Menthol	.14	.22
Borneol	.18	.74
Cyclohexanol	.17	.58
Methylcyclohexanol	.14	.17
Diethylaminoethanol	.14	.56
Furfurylcarbinol	.21	.34
Dimethylhexenol	.18	.38

4

ALLYL BROMIDE (3-Bromopropene; 3-Bromopropylene; Bromoallylene.)



$H_2C=CH-CH_2-Br$

Molecular weight 120.99
Synthesis, see Ref. 1746

GENERAL

In tests of 309 aliphatic compounds, evaluated as insecticidal fumigants, allyl bromide stood 10th in order of 2670
effectiveness. Halogen substitution in the lower aliphatic hydrocarbons yields a number of effective insecticidal 3390
fumigants. Among the volatile, halogenated fumigants, bromine analogues generally compare favorably with, 2537
and may even surpass in effectiveness, the corresponding chlorinated compounds in toxicity to insects. For example, ethylene dibromide, q.v., is somewhat more toxic than ethylene dichloride for Tribolium confusum. The weakness of allyl chloride as an insecticidal fumigant is inflammability.

PHYSICAL, CHEMICAL

A clear, colorless liquid; toxic, irritating, penetrating, pungent, of unpleasant odor; inflammable; m.p. -119°C; b.p. 71.3°C; $d_{4°}^{20°}$ 1.398; $n_D^{20°}$ 1.46545; highly volatile; slightly soluble in water; miscible with many organic solvents; for example, alcohol, chloroform, ether, carbon disulfide, carbon tetrachloride. Containers should be kept tightly closed.

TOXICOLOGICAL

1) Toxicity for higher animals:
   - a) Stands among the most toxic of the halogenated hydrocarbons. 12,3211
     - (1) When exposed at concentrations of 100, 50, 20, 10 mg/l, rats and Guinea pigs show, in but few minutes, intense irritation of mucous membranes.
     - (2) Lung and liver lesions, general slight liver changes follow exposure.
     - (3) For rats, Guinea pigs narcotic action is weak.
     - (4) Some deaths have occurred among rats, Guinea pigs exposed for 4 hours to concentrations as low as 1 mg/l.
     - (5) Death is apparently caused by lung injury and possibly by kidney damage. Survivors, however, procede to complete recovery.
     - (6) For man, the odor, intense irritation, lachrymatory properties should make allyl bromide amply self-warning.
     - (7) No industrial poisonings have been recorded for either allyl bromide or allyl chloride.
     - (8) Maximum allowable concentrations have not been established.
   - b) In man, exposed to allyl bromide, irritation of the mucous membranes of eyes, nose, respiratory tract and lungs has been observed. Vertigo has been noted. 1045

c) Tests of toxicity using rats, Guinea pigs; five animals/test group: 12

Rats				Guinea Pigs			
Conc. mg/l	Exposure hrs	Dead no.	Survivors no.	Conc. mg/l	Exposure hrs.	Dead no.	Survivors no.
1	2	0	5	1	1	0	5
1	3	0	5	1	2	1	4
1	4	1	4	1	3	0	5
1	6	1	4	1	4	5	0
1	7	0	5	1	6	5	0
1	8	5	0	1	9	5	0
1	9	5	0	10	0.5	0	5
10	0.5	0	5	10	1	0	5
10	1	0	5	10	2	5	0
10	2	4	1	50	0.166	0	5
10	2	2	3	50	0.25	0	5
10	3	5	0	50	0.5	2	3
10	4	5	0	50	0.5	5	0
20	0.5	0	5	50	0.5	2	3
20	1	1	4	50	0.75	4	1
20	2	5	0	50	1	5	0
50	0.5	0	5				
50	1	4	1				
50	1.25	5	0				
50	2	5	0				
100	0.25	0	5				
100	0.5	4	1				
100	0.5	5	0				
100	1	5	0				

2) Toxicity for insects:

a) Certain alkyl and aryl halides, among them allyl bromide, have on insects an irritant effect. Toxicity, however, is not necessarily a property of these substances. 2537

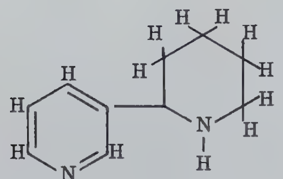
(1) Allyl bromide has high toxicity, as a fumigant, for those insects against which it has been tested.

b) Quantitative:

Insect	Route	Dose	Dosage mg/l	Exposure hrs	°C	Remarks	n-Butyl bromide $CH_3(CH_2)_3Br$ MLC, mg/l	
Sitophilus oryza	fumig	MLC	17	1	25	Empty flasks, 20 l.	382	3390
Sitophilus oryza	fumig	MLC	1	24	25	Empty flasks, 20 l.	22	3390
Sitophilus oryza	fumig	MLC	6	24	25	In wheat grain.	89	3390
Tribolium confusum	fumig	MLC	23	1	25	Empty flasks, 20 l.	318	3390
Tribolium confusum	fumig	MLC	3	24	25	Empty flasks, 20 l.	32	3390
Tribolium confusum	fumig	MLC	10	24	25	In wheat grain.	102	3390
Tribolium confusum	fumig	LC_{50}	9	5	25	Empty flasks.	—	3390
Limonius canus	fumig	LC_{50}	4.2	5	77°F	Flasks, 1l c̄ 500g soil.	—	1958
Limonius californicus	fumig	LC_{50}	4.2	5	77°F	Flasks, 1l c̄ 500g soil.	—	1958

5

ANABASINE [L-2-(3'-Pyridyl)-piperidine; Neonicotine (=DL form)]



Molecular weight 162.24
Synthesis [See Ref. 2930]

GENERAL [Refs: 2615,2854,2419,2855,2417,2418,1580,2856,2664,2665,2108]

An alkaloid, closely related to nicotine which it resembles in all its biological properties, isolated from the woody, perennial plant, Anabasis aphylla, Chenopodiaceae, whose alkaloidal content ranges from 1.0-2.6%, the greater concentration being found in young growth. May also be isolated from Nicotiana glauca, "tree tobacco," of alkaloidal content approximating generally 1.0% but reaching 8% in some biotypes and hybrids. Anabasine is extractable from plant tissues with water, dilute acid, ethylene dichloride, steam distillation. Synthesized as neonicotine in which anabasine, the L-rotatory racemer, accounts for most of the biological activity. Used insecticidally as anabasine sulfate.

Also consult Nicotine.

PHYSICAL, CHEMICAL

In the pure state, a viscous, colorless liquid, darkening rapidly in air; C = 74.03%, H = 8.7%, N = 17.27%; m.p. 9°C; b.p. 280.9°C; $d^{20°}$ 1.048; $n_D^{20°}$ 1.5443; v.p. 2.5 mm $Hg^{79°}$; $[\alpha]_D^{20°}$ -82.20; miscible, in all proportions, with water; soluble in most organic solvents (note its extraction from plant tissue by ethylene dichloride); alkaline in reaction, forming salts readily with acids, metals; stable. Commercial anabasine is said to contain: Anabasine 21.52%, lupinine 7.52%, aphylline, aphyllidine 10.45%, total sulfate 12.19%, sulfuric acid 1.68%, other substances 1.24%. Sold as anabasine sulfate in water solution. Chemically distinguishable from nicotine by precipitation from solution in methanol as the silicofluoride; nicotine remains in solution. The vapor pressure is sufficiently high to permit a short range fumigant action on insects.

TOXICOLOGICAL

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	
Guinea Pig	sc	LD_{50}	22	1319
Rabbit	iv	MLD	3	1319

- a) Six times as toxic as rotenone, q.v., and only slightly less toxic than nicotine for Caraussius auratus, gold fish. 1145, 2815
- b) Readily absorbed, like nicotine, through intact skin and mucous membranes.
- c) Residues of sprays, when used on food plants, are too evanescent to be hazardous.
- d) Symptoms of acute and sub-acute intoxication:
  - (1) Onset of symptoms after exposure is rapid. 2221,1145
  - (2) Signs: Increased salivation, giddiness, headache, nausea and vomiting, mental confusion, visual disturbances, photophobia, cold extremities, asthenia, rapid breathing, faintness, convulsions and clonic spasms. Death in respiratory failure.

2) Phytotoxicity:
- a) None reported.

3) Toxicity for insects:
- a) General remarks:
  - (1) Particularly effective vs. aphids; 5-10 times as toxic as nicotine vs. Aphis rumicis, = A. fabae, 1115,2606
  - (2) Order of toxicity for Aphis rumicis, based on LC_{50} as spray: Anabasine > L-β-nicotine = DL-β-nornicotine > DL-β-nicotine > DL-α-nicotine = DL-α-nornicotine. 2606
  - (3) Less toxic than nicotine vs. Culex pipiens (larva), Carpocapsa pomonella, Oncopeltus fasciatus. 457,2832
  - (4) More toxic than nicotine, nornicotine vs. cabbage, pea, Nasturtium aphids and Paratetranychus citri. 298
  - (5) Anabasine, applied to Aphis spp. as contact spray in alkaline medium, in which the alkaloid exists as free base, is twice as toxic as the equivalent solution of anabasine sulfate. 1642
  - (6) Inferior to nicotine as an intestinal poison for silkworm, grasshoppers. 353

b) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aphis rumicis	contact spray	LC_{50}	5 mg/100cc	With 0.25g Na oleate/100cc.	2606
Aphis rumicis	contact spray	LC_{100}	166 mg/100cc	With 0.25g Na oleate/100cc.	2606
Lygaeus kalmii*(eggs)	spray	LC_{50}	0.18%	S.E. = 0.01.	2858

*LC_{50}, nicotine = 0.11%, quinoline = 0.12%, piperidine = 0.29%, pyridine = 19.6%.

(1) Toxicity of anabasine (base), anabasine sulfate, vs. adult Scirtothrips citri on lemon tree leaves, by contact and fumigant action: 2182

Substance	Conc.	Dosage (cc/leaf)	Residue Age at Test Start (days)	Kill(%) in 1 day	2 days	3 days	4 days
Alkaloid in H_2O	1:1000	0.2	0	—	100	—	—
" " "	"	.2	2	29	60	—	—
" " "	"	.2	0	91	100	—	—
" " "	"	.2	1	94	100	—	—
" " "	"	.2	3	89	100	—	—
" " "	"	.2	5	—	—	90	
" " "	"	.25	0	90	100	—	—
" " "	1:1500	.25	0	99	100	—	—
" " "	1:2000	.3	0	57	67	77	78
Anabasine sulfate*	1:800	.25	0	91	100	—	—
" "	"	.25	2	93	98	98	100
" "	"	.3	0	—	100	—	—
" "	"	.3	0	100	—	—	—
" "	"	.3	2	—	93	100	—
" "	1:600	.3	0	—	100	—	—
" "	"	.3	2	98	99	100	—
" "	"	.3	5	94	95	97	99
CONTROL		—	—	—	—	—	1.7

*40% anabasine base.

(2) Anabasine sulfate (40% anabasine base) diluted 1:400 in water and used as a spray produced only 2% mortality among first instar larvae of Hippodamia convergens, a lady-bird beetle predator of aphids. 1450

c) Pharmacological, biological, physiological effects on insects:

(1) By analogy with nicotine, anabasine enters the insect body through the cuticular surface, the penetration being more rapid through the unsclerotized or relatively less sclerotized regions. Anabasine is a rapid contact poison for insects. 353, 2231, 2815,1059

(2) Penetration of undissociated anabasine through the cuticle of cast, empty, larval exoskeleta of Chironomus has been demonstrated; the results resemble closely those obtained with nicotine. 3049, 2604

(3) Anabasine, as a contact spray, in alkaline solution as the free base applied to Aphis pomi yielded twice the kill given by equivalent solutions of anabasine sulfate.

(4) The fumigant action of anabasine, like that of nicotine, permits entry into the insect via the spiracles as well as via the integument. 2607, 1204,2187

(5) The action of anabasine is neurotoxic, the site of action being the neuromuscular mechanisms. 353,2231

(6) With the central nerve cord intact the heart-rate of Pteronus ribesii larvae was increased four fold by anabasine; a lower rate of increase was noted in subjects with severed nerve cords. 3049

(7) Pteronus ribesii larvae, dipped in 0.5% anabasine solution, were paralyzed in 2-15 minutes after dipping; 1% solutions induced a marked but short term rise in respiratory rate. 2709

(8) Convulsive movements, followed in 7-10 minutes by paralysis, attended application of 1% anabasine sulfate to Pteronus ribesii larvae. Expulsion of fluid from mouth and anus indicated peristaltic gut disturbances. Applied directly to the ventral nerve cord of Pteronus and Pieris brassicae larvae, anabasine at concentrations as low as 0.00001% instantly halted pulsation of the dorsal blood vessel. 3049

(9) Contact application of anabasine to Scirtothrips citri yielded instant ataxia and convulsions; in 10 minutes paralysis ensued while slight leg tremor persisted for 2 days or until death. 1450

(10) Anabasine blocks nerve impulse transmission at the synapse, but at higher concentrations than nicotine. 1450

(11) Applied to a ganglion, anabasine "proofs" or renders it refractory to subsequent nicotine treatment. Apparently involved for both agents are the same tissue receptors or action sites. 3295

6

ANTIBIOTICS; ANTIMETABOLITES

Inclusion of data concerning the action on insects of compounds classed in the broad categories of antibiotics and antimetabolites is not meant to suggest that, as yet, practically useful insecticides have been found among them. The data are presented for their general toxicological interest.

1) Toxicity of microbial antibiotics applied by injection in water solution to adult Blattella germanica: 1993

Compound	Commercial Source	LD_{50} (μg/insect) ♂	LD_{50} (μg/insect) ♀
Dihydrostreptomycin SO_4	Squibb	38	50
Neomycin SO_4	Upjohn	27	60
Streptomycin SO_4	Squibb	70	130
Terramycin HCL	Pfizer	90	165
Bacitracin	Commercial Solvents	100	235
Penicillin G Sodium	Upjohn	350	400-500
Penicillin G Potassium	Bristol	300	400-500
Polymixin	Nutritional Biochemicals	11	23
Aureomycin*			

*Four 60μg injections, given every second day, were tolerated with negligible mortality. The substance is soluble only to 3%.

2) Chemical impairment of development in Musca domestica: 1849

a) Effects of various substances and classes of substances incorporated in CSMA larval rearing medium innoculated with eggs of Musca.

b) Classes of compounds: I = mitotic poison; II = antimetabolite; III = other biologically active substances.

Compound	Class	Conc. (% by wgt)	Extra Days to Pupation	Imago Emergence %
Ethyl carbanilate	I	0.25	1	0
Ethyl carbamate	I	.125	0	63
N, N-bis (2-Chloroethyl) methylamine HCl	I	.25	2	3
" " " " " " "	I	.0215	1	48
Sulfanilamide	II	.25	0	18
2-Pivalyl-1-indanedione	II	.0625	4	16
" " " "	II	.0313	4	2
2-Pivalyl-1-indanedione Sodium	II	.0313	3.5	33
p-Nitrophenol	II	.25	2	0
Benzimidazole	II	.25	3	43
p-Nitrobenzoic acid	II	.25	0	10
Menadione	III	.125	4	11
"	III	.0063	1.5	25
Piperonyl butoxide	III	.11	1	28

3) Compounds which yield complete inhibition of larval development in Musca domestica. Symbols for compound classes are the same as in the preceding table. 1849

Compound	Class	$LEC^{\dagger}_{100}$ (%)
Podophyllotoxin	I	0.122
Ethyl carbamate (urethane)	I	.25
Ethyl carbanilate (phenyl urethane)	I	.5
Colchicine	I	.063**
2-Pivalyl-1-indanedione Sodium	II	.063
2-Pivalyl-1-indanedione	II	.125
2-Isovaleryl-1,3-indanedione Sodium	II	.0313**
Coumarin	II	.25
Sulfanilamide	II	.5
p-Nitrophenol	II	.5
Thiourea	II	.025
N-2-Carboxyethyl diethyl phosphoramidothionate	III	.013
Pyridine	III	.125
Phenothiazine	III	.25
Menadione	III	.25
O,O-Dimethyl-2,2,2-trichloro-1-hydroxyethyl phosphonate	III	.0079

Compound	Class	LEC$_{100}^{\dagger}$ (%)
Diazinon	III	.0313
N-Carbethoxymethyldiethyl phosphoroamidothionate	III	.0063
N-Caprylcolaminoformylmethylpyridinium chloride*	III	.0313

*Quaternary NH_4 salt.
**Lowest concentration tested.
† Lowest effective concentration for complete inhibition of development.

7

ARSENIC AND ARSENICALS, GENERAL TREATMENT

GENERAL REMARKS

[Refs. 2815, 353, 1059, 757]

Arsenic trioxide, As_2O_3, and arsenic pentoxide, As_2O_5, yield, in water solution, two acids, arsenious acid, H_3AsO_3, and arsenic acid, H_3AsO_4. The salts of these two acids are, respectively, arsenites and arsenates. The two oxides, and numerous metallic arsenites and arsenates, are powerful insecticides long employed in agriculture. One arsenate, $FeAsO_4 \cdot 2H_2O$, is found in some localities of Utah as the mineral scorodite.

1) Arsenites:
   a) Arsenites are generally more soluble in water than the arsenates and more toxic to plants and animals. The arsenites are of three classes:
      (1) Orthoarsenites X_3AsO_3 (X = a monovalent metal)
      (2) Meta-arsenites $X\ AsO_2$
      (3) Pyroarsenites $X_4As_2O_5$
   b) Sodium arsenite:
      (1) Averages 82% arsenious acid and is looked upon as a solid solution rather than a definite chemical entity.
      (2) Usually sold as solutions with a strength of 32% AS_2O_3 or 4 pounds white arsenic equivalent per gallon, U.S.
   c) Paris Green:
      (1) The acetoarsenite of copper; As_2O_3 equivalent: 58.55% (theoretical), 54-57% (practical).
   d) Other arsenites in practical use or with good insecticidal action are:
      (1) Zinc arsenite (compatible with lime-sulfur)
      (2) Calcium arsenite
      (3) Acid copper arsenite
      (4) London purple, a mixture of calcium arsenite and calcium arsenate.

2) Arsenates:
   a) Arsenates are less active as insecticides than arsenites and show a lower phytotoxicity. They are of three classes:
      (1) Orthoarsenates (chief, in insecticidal interest)
      (2) Meta-arsenates
      (3) Pyroarsenates
   b) Lead arsenate:
      (1) Sold as a commercial product varying in As_2O_5 content from 31 to 33% having up to 0.25% water soluble arsenic. 60% of the weight is in lead.
      (2) Acid lead arsenate, $PbHAsO_4$, is the ordinary lead arsenate of commerce.
      (3) Basic lead arsenate, 4,1,3,1-lead hydroxyarsenate, $Pb_4(PbOH)(AsO_4)_3 \cdot H_2O$, is also of insecticidal value.
   c) Calcium arsenate:
      (1) The series corresponds to the lead arsenates but is more soluble in water; lead arsenate is 0.25% soluble, dicalcium arsenate, 60% soluble. The substance is a stable, basic arsenate.
      (2) From the system $CaO\text{-}As_2O_5\text{-}H_2O$ at 90°C the following are separable:
         Dicalcium arsenate, Ca_2HAsO_4
         Pentacalcium arsenate, $Ca_5H_2(AsO_4)_4$
         Tricalcium arsenate, $Ca_3(AsO_4)_2$
         Basic calcium arsenate, $[Ca_3(AsO_4)_2]_3 \cdot Ca(OH)_2$
      (3) Phytotoxicity depends largely on the dicalcium arsenate content, and heating, during manufacture, reduces the amount of water-soluble arsenic and decreases phytotoxic action.
   d) Other arsenates of interest include: Copper arsenate, $Cu(CuOH)AsO_4$, basic copper arsenate (As_2O_5 40.6%), ferrous arsenate, ferric arsenate, aluminum arsenate, zinc arsenate, barium arsenate.

3) Factors affecting toxicity of arsenicals:
  a) Solubility is the determinant factor in toxicity for plants and animals, other factors being:
    (1) Particle size, nature of the water, presence of other insecticides, additives, CO_2 content of water, air and plant-produced CO_2, pH of the medium or of the insect gut, all of which affect solubility.
    (2) In distilled water, acid lead arsenate hydrolyzes as follows: $5PbHAsO_4 + H_2O \rightarrow Pb_4(PbOH)(AsO_4)_3 + 2H_3AsO_4$, the reaction attaining equilibrium quickly and being driven to completion by removal of arsenic acid.
    (3) Lead arsenate is more soluble in hard water than in distilled water and solubility is enhanced by NaCl and Na_2CO_3. Chlorides, sulfides, carbonates, bicarbonates promote soluble arsenic formation.
    (4) Heavy fogs, dews, high relative humidity, poor drying conditions, airborne sea spray all promote phytotoxicity after application of arsenicals to plants.
  b) A qualitative comparison between 2 important arsenicals:

Lead arsenate	Calcium arsenate
Acid reaction	Basic reaction
Single chemical entity	Variable mixture
Bases release soluble arsenic from	Slight reaction with bases
Carbonates release soluble arsenic from	Acids release soluble arsenic from
Hard waters release soluble arsenic from	Carbonates release soluble arsenic from
CO_2 affects but little	Lime excess protects from hard H_2O
Resists weathering	CO_2 releases soluble arsenic from
Reacts with lime-sulfur.	Easily weathered. Compatible with lime-sulfur.

4) Toxicity of arsenic and arsenicals for insects:
  a) General considerations:
    (1) Arsenites are more rapid than arsenates in toxic action.
    (2) Trivalent and pentavalent forms do not differ significantly in toxicity.
    (3) Insecticidal action chiefly via alimentary tract absorption.
    (4) Significant contact action via cuticle under proper conditions.
    (5) Insect susceptibility may vary with age, for example, the variations in susceptibility shown by several instars of Bombyx mori.
    (6) Not all insects consume arsenicals readily; some are sickened before a toxic dose is taken and stop feeding. Popillia japonica adults, for instance, will not consume arsenicals and are repelled by them. 3178
    (7) Temperature may influence the mortality yielded by an arsenical as well as the length of time needed for killing action.
  b) Examples of species differences in arsenic susceptibility as related to route of entry; the amount of arsenic stated is in terms of arsenic element: 206

Route	LD_{50}, mg/k				LD_{95} mg/k			
	Apis mellifera	Popillia japonica	Oncopeltus fasciatus	Galleria mellonella	Apis	Popillia	Oncopeltus	Galleria
Parenteral	0.8	6.6	3.4	7.5	4.6	34	8.8	9.2
Enteral	.0046	9.8	—	8.9	.0049	28.6	—	17.5
Topical	—	> 1721.0	88	> 3014.0	—	*	879	*

*Exceeded the maximum measurable dose.

(1) Order of susceptibility based on LD_{50}: 206

Parenteral	Apis > Oncopeltus > Popillia > Galleria
Enteral	Apis > Galleria > Popillia
Topical	Oncopeltus > Popillia > Galleria

(2) Relative susceptibility by the most effective route; based on LD_{50}; most susceptible insect as 1: 206

Basis	Apis mellifera	Oncopeltus fasciatus	Popillia japonica	Galleria mellonella
LD_{50}	1	739	1435	1630
LD_{95}	1	1.9	2	6.2

(3) Order of effectiveness of various routes; based on LD_{50}: 206

Apis mellifera	Enteral > parenteral > topical.
Popillia japonica	Parenteral = (ca) enteral > topical.
Oncopeltus fasciatus	Parenteral > topical.
Galleria mellonella	Parenteral = (ca) enteral > topical.

(4) Relative toxicity of arsenic and certain other toxicants via most effective route; based on LD_{50}: 206

Toxicant	Apis	Popillia	Oncopeltus	Galleria
Arsenic	1	15	1	1
Parathion	17	1	2	12
Ethylene dichloride	10,435	71	962	411
DDT	43	208	89	10
Nicotine	11,304	1188	11	99

(5) Toxicity of arsenic and some other toxicants by each route; based on LD_{50}: 206

Route	Insect	Order of Toxicity (highest—lowest)
Parenteral	Apis	DDT arsenic parathion nicotine ethylene dichloride
"	Popillia	parathion arsenic DDT nicotine ethylene dichloride
"	Oncopeltus	arsenic parathion nicotine DDT ethylene dichloride
"	Galleria	arsenic DDT parathion nicotine ethylene dichloride
Enteral	Apis	arsenic parathion DDT
"	Popillia	parathion arsenic DDT nicotine ethylene dichloride
"	Oncopeltus	
"	Galleria	arsenic parathion DDT nicotine, ethylene dichloride
Topical	Apis	parathion arsenic DDT nicotine ethylene dichloride
"	Popillia	parathion DDT nicotine ethylene Cl_2 arsenic
"	Oncopeltus	parathion arsenic DDT nicotine ethylene dichloride
"	Galleria	parathion nicotine DDT arsenic ethylene dichloride

c) Oral LD_{50} of several arsenicals for various insects:

Compound	Insect	Dosage	
Arsenic trioxide	Bombyx mori, 4th instar	0.015-0.02 mg/g	455
" "	Musca domestica, adult	0.18 mg/g	2463
" "	Melanoplus femur-rubrum	0.137 mg/g	1742
" "	" " "	ca. 0.36 mg/g	2611
" "	Melanoplus bivittatus	0.026 mg/g	2611
" "	Melanoplus differentialis	0.09 mg/g	2611
Arsenic pentoxide	Bombyx mori, 4th instar	0.02-0.04 mg/g	455
Sodium arsenite	Melanoplus bivittatus, adult	0.015 mg/g*	2611
" "	M. femur-rubrum, adult	0.1 mg/g	2611
Aluminum arsenate	Bombyx mori, 4th instar	0.9 mg/g	459
Zinc arsenite	Ascia rapae	> 1.99 mg/g	1381
Manganese arsenate	Datana ministra	0.15 mg/g**	1381
Acid lead arsenate	Alabama argillacea	0.02 mg/g	1103
" " "	Yellow necked caterpillar	0.05 mg/g	1381
" " "	Catalpa sphinx moth, larva	0.062 mg/g	387
" " "	Leptinotarsa decemlineata, 5th instar	0.08 mg/g; 0.3 mg/g	1743,2609
" " "	Bombyx mori, 4th instar	0.086 mg/g	387
" " "	Bombyx mori, larva full grown	0.0273 mg/larva***	586
" " "	Pieris rapae, 5th instar	0.09 mg/g	1742
" " "	Pieris rapae, 5th instar	0.1 mg/g	944
" " "	Anticarsia gemmatilis, 5th instar	0.11 mg/g	943
" " "	Prodenia eridania, 5th instar	0.14 mg/g	944
" " "	Malacosoma americana, last instar	0.15-0.21 mg/g	387
" " "	Heliothis armigera, larva	0.17 mg/g; 0.26 mg/g	1381,1742
" " "	Cirphis unipuncta, larva	0.25 mg/g	1742
" " "	Melanoplus differentialis, adult	2-4 mg/g	2617
" " "	Apis mellifera, adult	0.0043 mg/g	2541
" " "	Apis mellifera, adult	0.0005 mg/bee*** = .5 µg/bee.	586
" " "	Apis mellifera, adult	5.0 µg/bee****	231
Sodium arsenate	Apis mellifera, adult	1.8 µg/bee****	1852
Calcium arsenate	Apis mellifera, adult	0.7 µg/bee****	1852

*Survival time after 0.4 mg/g = 20 hours.
**0.01-0.25 = intermediate zone.
***MLD as arsenic, per se.
****As arsenic, per se.

d) Quantitative toxicity of sodium and lead arsenates: 2219,2220

Compound	Insect	Route	LD_0 (µg/g)	LD_{50} (µg/g)	LD_{100} (µg/g)
Sodium arsenate	Anasa tristis, adult*	inj	10	20	40
($Na_2HAsO_4 \cdot 7H_2O$)	Ceratomia catalpae, larva**	inj	10	20	30
"	Periplaneta americana, adult ♂	†topical	30	100	300
"	" " " ♀	††topical	—	500	1300
"	" " " ♂	topical	—	ca100	—
"	" " " ♀	topical	—	>1600	—
"	" " " ♂	or	80	250	600
"	" " " ♀	or	600	2000	6000
"	" " " ♂	inj	23	30	45
"	" " " ♀	inj	35	50	70
"	" " " ♂	inj***	—	ca25	—

d) Quantitative toxicity of sodium and lead arsenates (continued)

Compound	Insect	Route	LD$_0$ (μg/g)	LD$_{50}$ (μg/g)	LD$_{100}$ (μg/g)
($Na_2HAsO_4 \cdot 7H_2O$)	Periplaneta americana, adult ♀	inj***	—	ca42	—
"	" " " ♂	inj†††	—	<50	—
"	" " " ♀	inj†††	—	ca500	—
"	Popillia japonica, adult	topical #	400	850	1700
"	" " "	inj	20	50	100
Acid lead arsenate	Periplaneta americana, adult ♂ †	topical	200	500	1300
(colloidal)	" " " ♀ ††	topical	400	1200	2100
" " "	" " " ♂	or	50	150	600
" " "	" " " ♀	or	150	400	1000
" " "	" " " ♂	inj	200	300	750
" " "	" " " ♀	inj	300	750	1400

*Average weight per insect: 0.126 (0.08-0.16)g.
** " " " " : 1.5 (1.0-2.3)g.
† " " " " : 0.9 (0.7-1.15)g.
†† " " " " : 1.3 (1.0-1.9)g.
***Bloodstream injection.
†††Stomach injection.
#Average weight per insect: 0.096 (0.07-0.14)g.

e) Toxicity of various arsenic compounds for 4 insect species; oral route: I = Leptinotarsa decemlineata (4th instar, av. wgt. 0.075g); II = Heliothis armigera (5th instar, av. wgt 0.315g); III = Pieris rapae (5th instar, av. wgt. 0.074g); IV = Melanoplus differentialis (av. wgt. ♂ 0.88g, ♀ 1.45g): 108

(1)

Compound	LD$_{50}$ ± 5% limits (mg/g)				
	I	II	III	IV	
Copper hydroarsenate	0.13±.019	—	0.45±.07	♀ 0.16±.055	♂ 0.11±.051
Copper hydroarsenate-arsenite	0.25 (extra polation)	—	0.24±.02	♀ 0.10±.053	0.068±.024
Lead arsenate	0.073±.011	0.17±.038	0.21±.07	—	
Calcium arsenate	0.052±.008	0.21±.083	—	0.18±.12	0.16±.086
Paris green	0.035±.015	0.023±.006	0.013±.003	—	—
P. green + Cuarsenate	0.051±.01	—	—	0.048±.016	0.022±.01
Cupric meta-arsenate	0.040±.008	—	—	—	—

(2) Relative speed of action of various arsenic compounds vs. Diabrotica duodecempunctata adults measured as minutes required after application to yield 50% kill. Toxicants applied by rolling insects in 1 gram of dust for 10 seconds.

Compound	Concentration Arsenic Compound			
	25%	50%	75%	100%
Copper hydroarsenate	250 min.	145 min.	135 min.	100 min.
Copper hydroarsenate - arsenite	195 "	125 "	90 "	80 "
Lead arsenate	600 "	365 "	310 "	245 "
Calcium arsenate	210 "	145 "	90 "	80 "
Paris green	225 "	95 "	65 "	55 "
Paris green - Copper arsenate	180 "	140 "	65 "	60 "
Cupric meta-arsenate	205 "	150 "	125 "	85 "

f) Relative toxicity of arsenites, arsenates for Rhagoletis by mouth: 2259

Insect		As Elemental Arsenic (mg/g)			
		Lethal dosage	Intermediate zone	Sublethal zone	LD$_{50}$
Rhagoletis pomonella	Na_3AsO_3	0.16-0.32	0.051-0.15	0.016-0.048	0.10
" "	Na_3AsO_4	0.15-0.30	0.037-0.14	0.007-0.036	0.009
Rhagoletis cingulata	Na_3AsO_3	0.11-0.34	0.042-0.10	to 0.023	0.08
" "	Na_3AsO_4	0.09-0.20	0.047-0.09	0.02 -0.045	0.07
Rhagoletis fausta	Na_3AsO_3	0.14-0.37	0.029-0.12	0.006 -0.027	0.07

g) Relative speed of action of various arsenic compounds vs. Rhagoletis, measured as mean hours required after application to yield 50% kill. Deposits from solutions or suspensions made up to contain 1g/100cc: 2259

Compound	Insect	Mean Hours
Lead arsenate	R. pomonella	165
" "	R. fausta	90
Calcium arsenate	R. pomonella	76
" "	R. fausta	62
Magnesium arsenate	R. pomonella	240
Sucrose (Control)	" "	310
" "	R. fausta	250

h) Relative toxicity of arsenites, arsenates vs. Bombyx mori (=I), Hyphantria cunea (=II), Malacosoma americana (=III), Apis mellifera (=IV). Toxicants as solutions and/or suspensions made to contain 0.076g of As_2O_3 or As_2O_5 equivalent per 100cc: 586

Compound	% Mortality In																			
	3 days					6 days					10 days					Toxicity for				
	I	II	III	IV	Av	I	II	III	IV	Av	I	II	III	IV	Av	I	II	III	IV	Av
Acid Pb arsenate	91	11	18	21	35.3	100	72.8	82.2	58	78.3	—	99.3	100	—	99.8	97	61	66.8	39.5	66.1
Sodium arsenate	99	28.8	36.6	33	49.3	100	72.2	91.4	62	81.4	—	96.6	100	—	98.9	99.7	65.9	76	47.5	72.3
Arsenate average	95	19.9	27.3	27	42.3	100	72.5	86.8	60	79.9	100	98	100	—	99.3	98.3	63.5	71.4	43.5	69.2
Zinc arsenite	96	12.5	68.9	25	50.6	100	37.5	96.9	44	69.6	—	60.9	100	—	87	98.7	37	88.6	34.5	64.7
Paris green (1)	100	30.7	65.7	15	52.8	—	85.2	99	62	86.6	—	100	100	—	100	100	72	88.2	38.5	74.7
" " (2)	100	38.9	59.3	25	55.8	—	86.7	97.5	55	84.8	—	100	100	—	100	100	75.2	85.6	40	75.2
" " (3)	98	18.5	53.9	22	48.1	100	72.3	97.6	57	81.7	—	96.6	100	—	98.9	99.3	62.5	83.8	39.5	71.2
Arsenite average	98.5	22.7	61.9	21.8	51.8	100	70.4	97.7	54.5	80.7	100	89.4	100	—	96.5	99.5	60.8	86.5	38.1	71.5
London purple (arsenate + arsenite)	98	24.1	34.7	11	42	100	57.1	92	33	70.5	—	94.7	100	—	98.2	99.3	58.6	75.6	22	63.9
CONTROL	0	0	0.6	0		0	0	8.8	12		0	2.6	23.1							

i) Relative toxicity of arsenates vs. Bombyx mori (=I), Hyphantria cunea (=II), Hyphantria textor (=III), Apis mellifera (=IV), Malacosoma americana (=V). Solutions and/or suspensions made to contain 0.076g As_2O_5 equivalent per 100cc: 586

Compound	% Mortality In											
	3 days						6 days					
	I	II	III	IV	V	Av	I	II	III	IV	V	Av
Acid Pb arsenate	91	29.9	47.6	21	18	41.5	100	95.3	84.2	58	82.2	83.9
Barium arsenate	22	3.2	10.9	11	14	12.2	68	68.2	37.3	18	75.1	53.3
Copper Ba arsenate	61	10	11.7	9	18.1	22	98	67.5	57	28	83.2	66.7
Magnesium arsenate	91	13.8	5.2	4	—	—	100	85.2	46.5	31	—	—
Aluminum arsenate	—	4.7	7.5	—	—	—	—	80.8	33.6	—	—	—
CONTROL	0	0	0	0	0.6		0	0.8	8.5	12	8.8	

Compound	10 days					Toxicity for					
	I	II	III	IV	Av	I	II	III	IV	V	Av
Acid Pb arsenate	—	100	100	100	100	97.	75.1	77.3	39.5	66.8	71.1
Barium arsenate	92	88.2	72.1	99	87.8	60.7	53.2	40.1	14.5	62.7	46.2
Copper Ba arsenate	100	95.2	82.7	100	94.5	86.3	57.6	50.5	18.5	67.1	56
Magnesium arsenate	—	100	83.8	—	—	97	66.3	45.2	17.5	—	—
Aluminum arsenate	—	98.3	80.9	—	—	—	61.3	40.7	—	—	—
CONTROL	0	24.7	16.9	23.1							

j) Relative toxicity of commercial lead and calcium arsenates vs. Bombyx mori (=I), Hyphantria cunea (=II), Malacosoma americana (=III), Leptinotarsa decemlineata (=IV), Melanoplus differentialis (=V). Expressed as net kill (%) after deducting % kill of normally fed controls. Solutions and/or suspensions made to contain 0.076g As_2O_5 equivalent per 100cc: 586

Compound		% Mortality In											
		3 days						6 days					
		I	II	III	IV	V	Av	I	II	III	IV	V	Av
Acid Pb arsenate		96	39.1	53.1	61.5	37.6	57.5	100	91.7	86.5	72.3	31.1	76.3
Basic Pb arsenate		61.3	8.5	53.6	47	33	40.7	81.6	45	88.5	66.2	31.6	62.6
Calcium arsenate		96	12	54.3	67.5	63.6	58.8	100	69.1	89.6	66.9	32.6	71.6
Calcium arsenate	range	12.5	1.1	43.9	45.6	42.6	30.7	18.7	15.6	81.4	47	32.6	41.8
(5 other commer-		|	|	|	|	|	|	|	|	|	|		|
cial samples)		72.5	4.3	60.3	60.5	62.4	51.1	96.1	42.1	87.6	73.3		62.6
CONTROL (not fed)		12.2	0	.4	20.1			61.2	28.6	15.3	43.7		
CONTROL (fed)		0	0	1.9	14.6	35.5	10.4	0	.7	5.5	20.7	67.4	18.9

Compound		10 days						20 days				Av. Toxicity
		I	II	III	IV	V	Av	I	II	III	IV	
Acid Pb arsenate		—	84.5	87.3	52.5	100	81.1	—	100	100	100	71.6
Basic Pb arsenate		96	74.8	87.5	47	100	76.3	100	100	100	100	59.9
Calcium arsenate		—	84	82.7	53.7	100	81.3	—	100	100	100	
Calcium arsenate	range	22.9	22.2	84.7	40.6	100	45.8	29.2	20.5	100	100	39.9
(5 other commer-		|	|	|	|		|	|	|			|
cial samples)		100	69.4	87.7	53.2		77.1	100	51.9			63.6
CONTROL (not fed)		71.5	83.3	78.3	37.4			100	100	100	100	
CONTROL (fed)		0	14.4	12.3	42.5	78.3	17.3	0	41.8	50.5	57.1	

k) Relative toxicity of pure oxides of arsenic and various other arsenic compounds. Net mortality (%) after deducting the % mortality among normally fed controls. Solutions and/or suspensions made to contain 0.076g of As_2O_3 or As_2O_5 equivalent per 100cc. *Bombyx mori* = I, *Hyphantria cunea* = II, *Malacosoma americana* = III, *Leptinotarsa decemlineata* = IV: 586

Compound	% Mortality In									
	3 days					6 days				
	I	II	III	IV	Av	I	II	III	IV	Av
Arsenic trioxide	40	21.6	4.6	19.2	21.4	58	67.3	50.5	23.1	49.7
Arsenic pentoxide	100	23.1	68.1	65.1	64.1	—	77.6	85.2	65.0	82.0
Calcium oxide	0	0	0	0.1	0	0	0	0	0.7	0.2
Calcium arsenate	96	12.5	54.3	64.8	56.9	100	69.2	89.6	63.4	80.6
Lead oxide	12.8	0	0	30.5	10.8	31.9	0	1.5	46.3	19.9
Acid lead arsenate	96	39.1	53.1	50.4	59.6	100	91.8	86.5	51.2	82.4
Zinc oxide	0	0	0	4.3	1.1	0	0	0	12	3
Zinc arsenite	85.7	4.8	73.8	59.8	56.0	98.0	32.7	90	58.9	69.9
Magnesium oxide	0	0	—	5.1	—	0	0	—	5.5	—
Magnesium arsenate	96	7.2	—	73.8	—	100	51.6	—	70.3	—
Copper oxide	0	0	—	0	—	0	0	—	0	—
Paris green	100	18.7	—	65.7	—	—	67	—	64.9	—
Copper Ba arsenate	—	10	—	63.1	—	—	66.9	—	68.9	—
Barium oxide	—	0	—	0	—	—	0	—	4.1	—
Barium arsenate	—	4.3	—	57.9	—	—	43.7	—	63.4	—
Control (not fed)	12.2	0	0.4	—	—	61.2	28.7	15.3	—	—
Control (fed)	0	0	1.9	14.6	4.1	0	0.6	5.5	20.7	6.7

Compound	10 days					20 days					Av Toxicity
	I	II	III	IV	Av	I	II	III	IV	Av	
Arsenic trioxide	70	95.6	78.9	—	67.1	86	100	100	35.1	94.6	46.1
Arsenic pentoxide	—	94.2	87.6	—	83.4	—	100	100	100	100	76.5
Calcium oxide	0	0	1.1	—	0.3	0	0	0	1.7		0.2
Calcium arsenate	—	92.7	87.7	—	83	—	100	100	100	100	73.5
Lead oxide	46.8	0	4.8	—	24.3	100	4.1	0	100	65.3	18.3
Acid lead arsenate	—	93.7	87.3	—	81.6	—	100	100	100	100	74.5
Zinc oxide	2	0	0	—	3.8	6	0	0	24.1	35	2.6
Zinc arsenite	100	66.7	86.9	—	74.8	—	70.2	100	100	97.8	66.9
Magnesium oxide	0	1.3	—	—	—	0	2.2	—	8.6	29.6	—
Magnesium arsenate	—	84.7	—	—	—	—	74.8	—	100	97.9	—
Copper oxide	2	0	—	—	—	2	2.5	—	0	27	—
Paris green	—	93.7	—	—	—	—	100	—	100	100	—
Copper Ba arsenate	—	91.1	—	—	—	—	100	—	100	100	—
Barium oxide	—	6.4	—	—	—	—	7.7	—	8.7	47.2	—
Barium arsenate	—	66.9	—	—	—	—	66.3	—	100	93.7	—
Control (not fed)	71.5	93.6	79.3	—	—	100	100	100	—	100	—
Control (fed)	0	4.1	12.3	—	14.7	0	21	50.5	57.1	32.2	

l) Relationship between toxicity and amount of arsenic rendered soluble by the insect. Analysis of dead and dying insects made 24 hours after feeding commercial and laboratory prepared arsenic compounds. *Apis mellifera* = I, *Bombyx mori* = II, *Ceratomia catalpae* = III; 586

Compound	% Arsenic								
	sol* in H_2O (control)	sol* in bodies of				made sol* in juices of			
		I	II	III	Av	I	II	III	Av
Acid lead arsenate (comm)	17.3	44.5	46	83.5	58.0	27.2	28.7	66.2	40.7
Basic lead arsenate (comm)	7.2	28.8	37.7	63.5	47.3	21.6	30.5	56.3	36.1
Calcium arsenate (comm)	35.7	78.6	60.6	84.7	74.6	42.9	24.9	49	38.9
Arsenic trioxide (comm)	5.2	64.8	33.9	20	39.6	59.6	28.7	14.8	34.4
Barium arsenate (lab)	30.5	69.4	30.3	64	54.6	38.9	0	33.5	24.1
Calcium meta-arsenate (lab)	2.4	41.8	39.1	22.6	34.5	39.4	36.7	20.2	32.1
Paris green (comm)	15.9	98.3	44.3	71	71.2	82.4	28.4	55.1	55.3
Paris green + lime	11.0	91.8	37.4	61.2	63.5	80.8	26.4	50.2	52.5
Magnesium arsenate (comm)	37.9	80.3	59.9	98.7	79.6	42.4	22	60.8	41.7
London purple (comm)	33.2	84.3	48.4	95.1	75.9	51.1	15.2	61.9	42.7
Zinc arsenite (comm)	6.0	58.4	63.8	73.9	65.4	52.4	57.8	67.9	59.4
Copper Ba arsenate (lab)	6.2	74.6	59.2	58.8	64.2	68.4	53	52.6	58.0
Arsenic pentoxide (pure)	100	88.4	70.9	89.6	83	—	—	—	—
Sodium arsenate (lab)	100	73.4	54.4	89.7	72.5	—	—	—	—

Compound	Toxicity based on I, II	H_2O Sol* As based on total As in sample (%)	Av amt As/insect analyzed (mg) I	II	III	Av
Acid lead arsenate (comm)	78.5	0.61	.0223	.1212	.0126	.052
Basic lead arsenate (comm)	61.7	1.73	.0142	.0803	.0158	.0368
Calcium arsenate (comm)	65.5	.20	.0099	.1245	.0189	.0511
Arsenic trioxide (comm)	69.5	38.0	.0091	.0914	.0285	.043
Barium arsenate (lab)	51	.68	.0105	.0694	.0138	.0312
Calcium metaarsenate (lab)	17.5	.04	.0120	.0676	.0160	.0302
Paris green (comm)	79.5	3.52	.0087	.1203	.0143	.0478
Paris green + lime	66.7	3.52	.0075	.1157	.0276	.0503
Magnesium arsenate (comm)	71	4.64	.012	.1460	.0173	.0584
London purple (comm)	73.7	5.3	.0068	.1315	.0305	.0563
Zinc arsenite (comm)	77.5	1.25	.0132	.1430	.0220	.0594
Copper Ba arsenate (lab)	66	6.27	.0058	.0675	.0177	.0303
Arsenic pentoxide (pure)	78.5	100	.0165	.1130	.06	.0632
Sodium arsenate (lab)	82.4	100	.018	.0968	.0169	.0439

*Sol = soluble.

(1) Calcium meta-arsenate is the least soluble and arsenic pentoxide is the most soluble of the tested compounds in the insect body. 586

(2) Arsenic pentoxide and sodium arsenate, although totally water soluble before ingestion, were recovered only to 75% as water soluble As. 586

(3) The greater the per cent of As made soluble by the insect juices, the greater is the toxicity rate of an arsenic-containing compound. 586

(4) Percentage of water soluble As in original samples is unrelated to toxicity save in the case of compounds completely water soluble. 586

(5) In general the greater the average amount of As in the insects analyzed the higher is the toxic rate of that arsenical. 586

(6) Using average weights of undried insects fed on all 14 arsenic compounds and the average arsenic content per insect: 586

Insect	Average Wgt (mg)	Arsenic Content (mg)
Apis	98	0.0119
Bombyx	1370	0.1063
Ceratomia	1620	0.0219

(7) None of the water extracts of arsenic-fed insects showed alkaline reaction, and the highest acid reaction was pH 5.8; average pH, 14 arsenicals: 586

Apis	pH6.0
Bombyx	pH5.7
Ceratomia	pH6.1

m) Relation of the quantity of water-soluble arsenic to the toxicity of various arsenic compounds. Test insects: *Bombyx mori* = I, *Hyphantria cunea* = II, *Malacosoma americana* = III, *Leptinotarsa decemlineata*, larva = IV, *Melanoplus differentialis* = V, *Hyphantria textor* = VI. Comm = commercial product, lab = laboratory grade, pure = chemically pure: 586

Compound	Insects	Water Soluble As Based On Total As	Net Toxicity (%) After Deduction of Control Mortality
Basic lead arsenate (lab)	I, II, III, IV	1.15	21.5
" " " (comm)	"	1.73	60.9
Acid lead arsenate (lab)	"	.57	59.6
Arsenic trioxide (pure)	"	17.77	46.1
Arsenic pentoxide (pure)	"	100	76.5
Zinc arsenite (comm)	"	1.25	66.9
Acid lead arsenate (new process)	I, II, IV	.69	66.9
" " " (comm)	I, II, III, IV, V	.61	68.9
Calcium arsenate (comm)	"	.41	70.0
" " "	"	.88	39.9
" " "	"	1.31	59.2
" " "	"	.20	60.1
" " "	"	.52	43.1
" " "	"	5.20	65.9
" " (lab)	"	.88	52.5
Calcium meta-arsenate (lab)	II, IV	.04	3.6
Monocalcium arsenate (lab)	"	89.26	81.2
Na arsenate + Bordeaux Mixt.	I, II, IV, V, VI	—	61.7
Paris green (comm)	"	3.52	65.5

m) Relation of the quantity of water-soluble arsenic to the toxicity of various arsenic compounds. Test insects: *Bombyx mori* = I, *Hyphantria cunea* = II, *Malacosoma americana* = III, *Leptinotarsa decemlineata*, larva = IV, *Melanoplus differentialis* = V, *Hyphantria textor* = VI. Comm = commercial product, lab = laboratory grade, pure = chemically pure: (Continued) 586

Compound	Insects	Water Soluble As Based on Total As	Net Toxicity (%) After Deduction of Control Mortality
Magnesium arsenate (comm)	II, IV, V, VI	4.64	50.2
Barium arsenate (lab)	"	.68	43.6
Copper Ba arsenate (lab)	"	6.27	48.9
Aluminum arsenate (lab)	II, IV, VI	1.91	39.3

(1) Pure arsenic pentoxide and laboratory mono-calcium arsenate, both readily water soluble, showed high insect toxicity; however some arsenic compounds, almost insoluble in water, showed toxicities almost as great. 586

(2) The toxicity of insoluble arsenic compounds does not seem to be based on the water-soluble arsenic present but rather on the stability of the particular substance and the ease of its breakdown in the insect body. 586

n) Amounts of arsenic consumed by certain insects in feeding tests involving various arsenic-containing compounds. Insects: *Hyphantria textor*, larva = I, *Leptinotarsa decemlineata*, larva = II. d = insects dried; wd = insects washed and dried: 586

Compound	mg As/larva Av.		As (ppm) In			Net Toxicity (mortality of control deducted)	
			larvae		feces		
	I	II	I	II	I	I	II
Acid lead arsenate	wd .0017	d .0017 (comm)	359	141	527	—	62.1
" " "	d .0025	d .0038 (lab	395	327	1114	68.6	57.9
Calcium arsenate (comm)	wd .0014	d .0026	303	205	746	—	62.7
" " "	d .0024	d .0026	481	—	1125	59.1	—
Basic lead arsenate (comm)	d .004	d .002	691	168	330	48.9	53.4
Calcium arsenate (lab)	d .0033	d .0043	436	311	851	15.1	61.8
Calcium arsenate + lime	d .004	d .0042	674	330	355	6.3	61.9
Barium arsenate (lab)	d .0027	d .0049	399	350	365	31.5	50.9
Magnesium arsenate (comm)	d .005	d .0029	747	223	539	36.5	57.1
Na arsenate + Bordeaux Mixt.	d .0016	d .0028	303	257	818	59.3	51.8
Zinc arsenite (comm)	d .0055	d .0018	917	172	903	63.6	54.7
Paris green (comm)	d .005	d .0024	911	206	946	62.6	59.5
Aluminum arsenate (lab)	d .0028	—	383	—	840	32.0	—
Copper Ba arsenate (lab)	d .0053	d .0051	613	460	306	41.8	54.7
CONTROL (feces)	—	—	—	—	15	—	

o) Toxicity of several arsenic-containing compounds, and various samples of such compounds tested as stomach poisons by feeding on dusted leaf squares to *Alabama argillacea*, 5th instar; note variations with compound, with sample, with particle size, etc.: 206

Compound	As_2O_3 (Total %)	As_2O_3 (H_2O sol %)	As_2O_5 (Total %)	As_2O_5 (H_2O sol %)	Dosage Range mg/g sublethal zone	intermed. zone	lethal zone	LD_{50} (mg/g)	Relative Toxicity*
Paris green (I.D. 3673)	58.4	2.33	—	—	(.001-.004)	(.01-.03)	(.04-.67)	.01	25
Calcium arsenate (I.D. 3672)	—	—	43.5	0.11	(.010-.06)	(.07-.46)	(.47-1.35)	.25	1
Paris green 3673 + Ca arsenate 3672									
I.D. 3678 P.g.**10: C.A.90***	—	0.38	45.4	0.10	.02	(.03-.08)	(.09-.34)	.04	6.3
I.D. 3738 P.g. 7.5: C.A. 92.5	5.06	—	44.72	0.03	(.02-.04)	(.05-.15)	(.16-.22)	.09	2.8
Calcium arsenate I.D. 3671	—	—	40.5	0.14	(.01-.08)	(.09-.21)	(.23-.52)	.18	1.4
" " I.D. 3737	—	—	42.1	0.03	(.01-.06)	(.07-.22)	(.23-.47)	.19	1.3
" " I.D. 3174	—	—	43.57	0.18	(.01-.06)	(.07-.15)	(.16-.72)	.12	2.1
" " I.D. 3208	—	—	41.0	0.11	(.04-.07)	(.08-0.2)	(.21-.41)	.18	1.4
" " I.D. 3209	—	—	43.14	0.11	(.03-.50)	(51-1.0)	(1.05-1.24)	.72	0.3
Lead arsenate I.D. 3674	—	—	31.1	0.22	(.004-.008)	(.01-.03)	(.04-.38)	.02	12.5

*Relative toxicity referred to calcium arsenate I.D. 3672 as the standard.

**P.g. = Paris green.

***C.A. = Calcium arsenate.

(1) Calcium arsenate 3174, coarsest particle size yielded 85% kill;
" " 3208, medium particle size " 64% ";
" " 3209, finest particle size " 27% " in cage tests vs. *Anthonomus grandis*.

(2) Calcium arsenate 3671 and 3737 are finer in particle size than 3208 but not as fine as 3209.

p) Toxicity for insects of organic arsenical compounds employed as stomach poisons:

(1) Data for 61 organic arsenicals tested vs. *Tribolium confusum* for insecticidal effectiveness is reviewed in Reference 1618.

5) Phytotoxicity:

a) Toxicity of various arsenic compounds for the cranberry bean, London horticultural variety, in humid 108
chamber tests. Leaves dipped in suspensions of arsenic compounds of various strengths:

Compound	% of Leaf Area Injured At Concentrations Of				
	0.05%	0.1%	0.125%	0.2%	0.3%
Copper hydroarsenate	trace	2	4	4	1
Copper hydroarsenate-arsenite	trace	1	5	8	2
Lead arsenate	trace	3	4	20	20
Calcium arsenate	19	56	65	53	72
Paris green	70	100	100	100	100
Paris green-Calcium arsenate	20	62	38	81	93
Cupric meta-arsenate	7	90	61	96	99

b) Soluble arsenic is intensely toxic to plants by any route of entry, therefor in insecticidal use on plants 2815
arsenic compounds are applied in as insoluble a form as possible. Sufficient solubilization of the arsenical in the insect body is depended upon to achieve insect killing. Still, insolubility does not entirely lift the phytotoxic hazard for any arsenical. Weathering and other influences may release soluble arsenic in phytotoxic amounts.

(1) Soluble arsenic may enter a plant via the leaf cuticle, principally where this is thinnest on the leaf 600
undersurface, via trunk, limbs, twigs (particularly if the bark is damaged) in which case death of a 1079
whole tree or of the affected limbs and twigs may ensue, or via the roots in trees especially if the 1463
upper roots are damaged. Permeability of the plant is enhanced by moisture, high humidity, lime, leaf 882
or bark wounds, and insect damage. Direct damage may be done to fruit and foliage by tissue plasmolysis.

(2) Arsenic acts on the plant as a protoplasmic poison which alters and impairs fundamental cell activities. 1463
Acute phytotoxicity is revealed by blackening of foliage and death of leaves, the older leaves being more 1079
susceptible. Basal foliage is killed before terminal foliage and chlorophyll is destroyed. Arsenic ab- 3025
sorbed from foliage is not translocated to the roots, while arsenic taken up from the soil is deposited 2981
chiefly in the leaves, reaching, in tolerant plants, very high levels. The usual symptoms of plant damage 2088
on apple trees and other pome fruits as examples are: Spot or marginal burning, necrosis, or red, 64
brown or purple discoloration. Leaf yellowing with the yellowing advancing from areas of spot damage followed by leaf-drop. Rapid absorption over the whole leaf surface yields quick leaf-drop.

(3) A rapid rise in respiration follows intake of arsenic by the leaf, with yellowing and leaf-drop ensuing if 2269
the rate increases by more than 50%. In oats, responding to arsenite in water at 1 ppm, transpiration de- 2301
clined. Sub-toxic amounts of arsenic may stimulate plants physiologically to promote growth and speed 1079
fruit maturity. 2981

(4) Any circumstance which increases the amount of soluble arsenic available for plant uptake enhances 2815
arsenical phytotoxicity. Temperatures above 80°F, humidity (fog, heavy dew), slow drying conditions, 97
application time, atmospheric chemicals, e.g. NaCl, CO_2, tend to enhance plant hazard. Soap increases 2743
hazard by promoting solubilization in "soft" waters but decreases hazard in "hard" waters.

(5) The peach tree is particularly sensitive to arsenic damage and shares this sensitivity with other drupes 2301
viz. the plum and cherry trees. Pomes, (apple, pear and quince trees) are arsenic sensitive. Beans, 2815
cucumbers, oats, and lettuce are highly sensitive plants. Grasses are, in general, resistant but some, 353
for example blue grasses, are sensitive. Most shade and ornamental trees are less sensitive than 2027
pomes but still susceptible to damage; even conifers may be harmed under certain conditions by calcium 3025
arsenate. 1311,97,2557

(6) Arsenites are in general more phytotoxic than arsenates but in each class variation exists. Lead arse- 2301
nate is least phytotoxic in orchard use, while calcium arsenate is most hazardous for such purposes. 1463
"Safening" substances are often combined with arsenic compounds to trim or minimize plant hazard. 618
Among such "safeners" are: Lime (for some), metallic oxides viz. ferric oxide, zinc sulfate, zinc 258
sulfate + lime. 2557,1191,1177,97,2116

(7) Accumulation of arsenic in the soil as a result of insecticidal application in orchards tends to be limited 1463
to the upper 8 inches of the soil bed. Arsenic becomes fixed in soils, the speed and proportion being 2700
influenced by soil type. Accumulated soil arsenic reduces productivity of soils, the yield of crops, 631
germination of seeds and growth, the degree of effect being roughly proportional to the soluble arsenic 353
in the soil. Such effects are well-known on certain old orchard soils. 618,3170,23,2981

PHARMACOLOGICAL, PHARMACODYNAMIC, PHYSIOLOGICAL, BIOCHEMICAL: INSECTS:

1) Arsenic compounds are for insects essentially "stomach" poisons, but they may exert contact action as well. 1973
In Periplaneta, exposed to sodium arsenite, absorption is via the midgut whence arsenic passes to haemolymph 970
and tissues. Periplaneta and Locusta have shown heavy arsenic concentration in midgut tissue with none in 1592
fore- and hind-guts.

2) Insect responses which affect or limit arsenic intake:

a) A repellent action is known for arsenicals; for example, sodium arsenite is avoided by some: Euxoa, 1592
Euproctis, Locusta migratoria. Locusta also avoids Paris green. 3190

b) In Euxoa, sodium arsenite inhibits, then produces, spasm of the anterior midgut sphincter which leads to 3206
vomiting. Pieris rapae larvae do not show this response.

c) Digestive sedatives, for example, bismuth subcarbonate, increase toxicity of lead arsenate for Popillia 2402
japonica.

d) The cathartic effect of some arsenicals leads to elimination of the poison before absorption. Sodium meta- 1592
arsenite, and Paris green are purgative for Euxoa and Pieris, costive for Locusta. Lead arsenate in- 3206
creases, As_2O_3 decreases food passage time in Periplaneta. 2917

3) Insect differences in arsenic absorption:
   - a) Euxoa larvae absorb much less intaken arsenic than Pieris and Locusta and pass less to the tissues. 3206
     35-40% of ingested arsenic appears in tissues of Pieris and Locusta, 20% in Euxoa. In Periplaneta 12% 970
     of arsenic (taken as sodium meta-arsenite) passes, ante-mortem, to the tissues. As^{76}, as $As_2^{76}O_3$, is only 2303
     slightly absorbed from gut by Tenebrio and Phlegethontius.

4) Efficiency of removal of As from the insect body:
   - a) High efficiency of removal via the Malpighian tubules is shown by Euxoa in which a 10-fold dosage increase 3206
     does not increase tissue arsenic as in Pieris, Locusta.

5) Effects of insect gut pH:
   - a) In Musca, arsenite solutions of various pH are equally toxic by ingestion. 2463
   - b) pH of the insect gut is a prime factor in toxicity. For example, Ca arsenate (solubility decreases to ca. zero 3108
     in alkaline media) is excreted unchanged from the gut (pH 8-9) of Bombyx mori larvae. For Dixippus, gut
     pH 6.6, Ca arsenate is an active poison.
   - c) Pb arsenate solubility is enhanced in alkaline media; thus for Carpocapsa pomonella, gut pH 8.5, although 3108
     it has 1/3 less As than Ca arsenate, it is equally toxic.
   - d) Arsenic salts of weak acids liberate free arsenic and arsenious acids. Phosphoric acid is the principal 1593
     insect gut acid; thus: Pb arsenate → Pb phosphate (insoluble) + arsenic acid (soluble) or arsenate ion. 3031
     The relative degree of dissociation to soluble arsenic in phosphate buffers at the gut pH of 9 insect species
     parallels the relative toxicities of Pb-, Ca-, and Mg- arsenates.
   - e) Soluble As, as dissociated arsenical ions, is less toxic than undissociated arsenic acids. For example, Na 814
     arsenite, Paris green are little toxic to some larval lepidoptera of gut pH 9.2-9.7, the arsenic being present
     consequently as dissociated salts. For Locusta migratoria, gut pH 6.8, acid radicals (thus undissociated
     Na arsenite and Paris green) show high toxicity.

6) Effects of temperature:
   - a) Prodenia eridania and Anticarsia gemmatilis larvae, fed Ca arsenate, acid Pb arsenate, or Cu arsenate 943
     and held at 60°F yielded a mortality 2-fold greater than at 80°F, although the mortality was later in development.

7) Symptoms of poisoning; sequential:
   - a) In Prodenia eridania larvae given Pb arsenate: Stopped eating, regurgitated, became inactive (followed 3349
     in some by temporary activity) died without convulsions.
   - b) In Blatta orientalis nymphs given As_2O_3: Watery diarrhoea, feeble movements, paralysis with spasmodic 1007
     twitching on stimulus, death.
   - c) In Periplaneta americana given arsenites, arsenates by injection: Decreased activity, loss of equilibrium 2327
     and of recovery reflexes, general asthenia, weak response to stimulus, no response to stimulus, death.
   - d) In Apis mellifera adults given As_2O_3 at 0.76 µg/bee: Average life was 5.4 days (controls 8.4 days); in- 2327
     activity with few deaths 2nd day after feeding; rapidly dying on 3rd day with swollen, dragging abdomens,
     staggering, inability to fly.

8) Histological, histopathological effects:
   - a) Prodenia larvae, 3 hours after oral poisoning by Pb arsenate while in the stage of feeble movement showed: 3349
     Cells of midgut epithelium in disintegration with loss of the striated border, dissolution of cell membrane,
     cytoplasmic vacuolization, nuclear changes with chromatin clumping, dispersion, dissolution. Similar responses attended Ca arsenate, Ca arsenite, As_2O_3. Paris green produced little histopathology.
   - b) Effects similar to the above followed Na and Ca arsenates but not Paris green in Vanessa larvae, Locusta 3349
     nymphs. Massive epithelial desquamation of midgut in Vanessa; in Locusta epithelial cell plasmolysis 2510
     and denudation stripping bare the basement membrane. 2439
   - c) Blatta, fed As_2O_3, showed decline in haemocyte count from 37,000 to 7000 per cc with elimination of the 1007
     large cell types. Similar effects noted in Locusta + the increase of small haemocytes and frequent mitosis. 2762
     In Schistocerca given Na arsenite by contact similar effects followed, also with frequent mitosis. Calliptamus yielded similar effects with, also, the presence of abnormally large haemocytes.
   - d) Blockade of haemocytes in Periplaneta enhanced arsenical toxicity suggesting these cells as a possible 3383
     detoxification site.
   - e) Arsenicals produced decline of blood volume due to water loss via alimentary hyper-secretion. 1592,2407

9) Physiological, biochemical effects:
   - a) Bombyx mori larvae fed Na arsenate showed decrease in heart rate; the same by injection brought increase 456
     in heart rate.
   - b) In Leptinotarsa: As produced no effect on digestive enzymes or the oxidases, peroxidases, or proteases of 998
     the Malpighian tubules whose ability to excrete salts remained unimpaired. 2459
   - c) As yields apparent damage to SH (sulfhydryl) containing enzymes. SH groups suggested as arsenite ion 3192
     receptors. Glutathione and cystein protect (mammals) against As. A marked decrease, 20-80%, of free 3193
     SH groups attends As intake. 999
   - d) Leptinotarsa larvae poisoned by arsenates or arsenites showed decreased O_2 consumption with Q_{10} increase. 997
   - e) Isolated Carpocapsa tissues in presence of Na arsenate showed 30-50% decline in O_2 uptake. 1243
   - f) Insect dehydrogenases are poisoned by arsenite. 2762,2846
   - g) At concentrations much greater than the decisive lethal dose in tissue preparations of Carpocapsa respira- 3385
     tory enzyme inhibition declined. An inflection in the concentration-effect curve (criterion: survival time)
     occurred for Blatta and Periplaneta given, by injection, $NaAsO_2$ and Na_2HAsO_4.

h) At low dosages, As has been found harmless and even "chemotherapeutic" for some larval lepidoptera. 2938

10) Trivalent and pentavalent As:
   a) Differences in toxicity between As^{+++} and As^{+++++} have been noted in some cases but not in others. Arsenite inhibits some enzyme systems which arsenate does not affect. Arsenate may partly replace phosphate in yeast glycolysis. 164
   b) For Malacosoma and Datana larvae arsenate is greatly less toxic than arsenite. 454
   c) As_2O_5 and Na arsenate proved less depressant to Leptinotarsa respiratory rate than As_2O_3 and Na arsenite. 997
   d) Vs. Apis mellifera and Locusta migratoria arsenite and arsenate are approximately equal in toxicity. 454,2439
   e) In arsenical poisoning, arsenates are believed to be reduced to arsenites. The toxicity of arsenates is increased by sulfite and by zinc dust which enhance reduction. 3107

TOXICITY AND HAZARD OF ARSENIC FOR HIGHER ANIMALS

1) Quantitative:

Animal	Route	Dose	Dosage	Remarks	
Man	or	Toxic	0.21-10 ppm	In water.	159,3379,960
Man	or	MLD	130 mg/average man	As As_2O_3 (100mg As perse).	446
Man	or	MLD	2 mg/k		2815
Man	or	LD	12 ppm	In water.	547
Rabbit	or	LD_{50}	20 mg/k	As As_2O_3.	1870
Rabbit	or	LD_{50}	100 mg/k	As lead arsenate.	1870
Rabbit	or	LD_{50}	50 mg/k	As calcium arsenate.	1870
Dog	or	LD_{50}	85 mg/k	As As_2O_3.	1870
Dog	or	LD_{50}	500 mg/k	As lead arsenate.	1870
Dog	or	LD_{50}	38 mg/k	As calcium arsenate.	1870
Pig	or	MLD	500 mg/animal	Arsenic element.	2593
Sheep	or	MLD	850 mg/animal	Arsenic element.	2593
Cow	or	MLD	2000 mg/animal	Arsenic element.	2593
Horse	or	MLD	2000 mg/animal	Arsenic element.	2593
Guinea Pig	or	MLD	14 mg/k	As lead arsenate.	2404
Laboratory Animals	or	MLD	5-100 mg/k	As As_2O_3.	2921
Mammals	or	MLD	100-500 mg/k	As lead arsenate.	1870
Fish	Medium	Toxic	1.1 ppm	Arsenic element.	2400,1050
Crappie	Medium	Toxic	15 ppm	Arsenic element.	3233
Bluegill	Medium	Toxic	15 ppm	Arsenic element.	3233
Minnow	Medium	Toxic	20 ppm	36 hrs exposure; Na arsenite.	1276
Minnow	Medium	Toxic	250 ppm	36 hrs exposure; Na arsenate.	1276
Bass	Medium	Harmless	6 ppm	Exposure ca. 10 days.	3233

   a) In drinking water, the following concentrations with long exposure have proved toxic: 0.21 ppm, 0.3 - 1.0 ppm, 0.4-10 ppm. 960 159,3379
   b) Fowl and pigs have succumbed to a single feeding containing 0.1 grain arenic per ounce of ration. However, in selenium poisoning, animals have been treated with 12-15 ppm arsenic in water. 5 ppm, as Na_2HAsO_3 has counteracted selenium poisoning in pigs and rats. 3103 2074 537

2) Chronic toxicity of arsenic:
   a) Save at high dosages, arsenic does not tend to be cumulative. Sheep have survived 500 mg/day and cattle and horses 2000 mg/day without development of symptoms. 2593
   b) In man, chronic arsenosis is slow of onset, not becoming patent for 2-6 years. In drinking water the following concentrations have been reported safe: 159 2954

	Refs.
0.05 ppm	[62,2400,1229]
0.1 ppm	[3089,3119,2272,159,1815]
0.15 ppm	[2400,960,2718]
0.15-0.25 ppm	[3119]
0.2 ppm	[62,2351]
1.0 ppm (temporarily)	[62]

   c) As employed in arsenical cattle-dips, arsenic is highly poisonous and has presented under some circumstances a high hazard. Arsenic may be absorbed through the unbroken skin and acute poisoning by this means has brought death in from 1-2 days. Less acute effects of poisoning have been skin blistering, cracking and peeling, diarrhoea, emaciation, anorexia, obvious signs of pain in the affected animals. Even a dip dosage normally deemed safe may in wet weather, or if animals are overheated, prove poisonous. Indiscriminate and careless voiding of arsenical cattle dips may seriously contaminate soil and water sources.

3) Residue hazards:
   a) Residue hazard of arsenicals is high. 353,2815
   b) Alfalfa fodder containing 650 ppm calcium arsenate has been fatal to cattle. 347
   c) Sprayed on alfalfa at 2 lbs/acre (residue = 10-90 ppm) presented no hazard. Cattle and sheep fed alfalfa sprayed at 3 lbs per acre showed no toxic signs. Decrease or halt in weight gain began with fodder sprayed at 6 lbs/acre. 1063

- d) Even on fodder sprayed at 8 lbs/acre with calcium arsenate (residue of 140 ppm) the intake of cows and horses (30 lbs forage) gives less than the 2000 mg of As_2O_3 which is tolerated. 2593
- e) Na arsenite residues have a higher hazard, being toxic or lethal to cattle feeding on grasses sprayed at 1.5 lbs/acre in locust control and receiving a total accumulated dosage of 4.2g (= to 2g As element). 2593
- f) Residues have been a problem for animals pastured in orchards treated yearly at 100 lbs/acre. At 25 lbs/acre chickens are unharmed, sheep show symptoms but recover, calves show mortality. At 8.5 lbs/acre calves are subject to anorexia. 2404
- g) Sheep, exposed to lead arsenate and excreting 2-5% of the intake, must accumulate 7g (1.5g As element) for fatality. 2983
- h) Residues on fruits have been considered a hazard to man. In England maximum permitted levels over the years have ranged from 0.025 grain/lb apples (as As_2O_3) to 0.01 grain (1.4 ppm)/lb apples to 3.6 ppm in 1940. Arsenic is not absorbed into the fruit itself but remains on the surface. Unless natural weathering reduces residue below danger level, washing of fruits in dilute acid is a necessary prelude to marketing. Wine made from arsenic-sprayed grapes, and oil from arsenic-sprayed olive trees are said to be arsenic-free. 353 1079

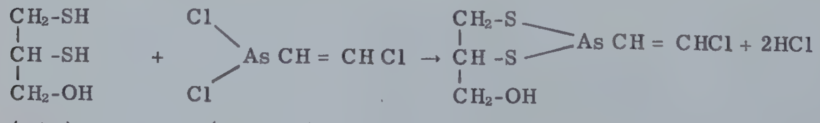
PHARMACOLOGICAL, PHARMACODYNAMIC, PHYSIOLOGICAL (HIGHER ANIMALS)

1) Trivalent arsenic (As_2O_3 for example) is an acute gastrointestinal irritant whose symptoms imitate those of cholera in some regards. 1220
   - a) Within one hour after intake a feeling of throat tightness and acute stomach pain ensue; vomiting becomes constant with blood in the vomitus; diarrhoea and excessive urination with blood in the stools and urine, follow; the skin is pale, chill; blood pressure declines; severe thirst is characteristic. Coma and death within the day attend acutely toxic intake.
   - b) Emergency measures: Emetics, lavage, purgation. Ferric hydroxide as antidote is useful only if given very early.

2) Symptoms of chronic arsenosis in man:
   - a) Pigment deposits about neck, armpits, eyelids; palmar and plantar hyperkeratosis, oedema of face and ankles; chronic diarrhoea; apathy and extreme dullness of mind. Half of the documented cases have shown keratosis and skin lesions predominantly, one fourth have exhibited gastric signs, one fifth have shown such neurotoxic signs as: Tremors, cramps, neuritis, paralysis and epileptiform fits. 1220
   - b) Arsenic-caused skin lesions have become cancerous and pre-cancerous; As_2O_3 is considered a carcinogenic agent. 3225

3) Acute poisoning in livestock:
   - a) Signs are ulceration and necrosis of stomach, depression, coma, a characteristic facies (horses especially). Calves have shown hindquarter paralysis advancing cephalad, rapid respiration, convulsions followed by death in tetany. 2593 2404
   - b) Sheep have tolerated arsenite dips of concentrations 0.2% (as As_2O_3). 60-90 mg are absorbed cutaneously but there is concomitant excretion via urine and saliva. 1527
   - c) Wound mortification may follow arsenic-containing dips. 725

4) Chronic poisoning in livestock:
   - a) Symptoms may begin with skin thickening and peeling. Calves have exhibited anorexia, asthenia, stiff joints, diarrhoea, cachexia. 2593 2404
   - b) Arsenic intoxication apparently does not exhibit marked or characteristic histopathology. Hepatic fatty degeneration and kidney pallor may follow more frequently after arsenates rather than arsenites. 353
   - c) Arsenic is eliminated via urine, faeces and other secretions and excretions; it may appear in the milk of exposed animals. Accumulation, when intake outstrips excretion, is chiefly in the liver and to a lesser extent in the kidneys. 2815 2593 446
   - d) Trivalent arsenic inhibits and has profound effects on cell respiratory mechanisms, being a protean and protoplasmic poison. 3224 3225
   - e) Arsenic combines with, and inhibits, free SH (sulfhydryl) groups and dehydrogenating enzymes (not as arsenate per se but must first be converted to arsenite for this effect). Cysteine and glutathione, SH containing substances, are protective. 3192 3193
   - f) 2,3-Dimercaptopropanol (BAL; British anti-Lewisite) is protective and chemotherapeutic in arsenic intoxication. BAL, given intramuscularly, increases the rate of As elimination. BAL controls skin lesions and other manifestations caused by trivalent As. The detoxification mechanism follows: 886 2489



$$\begin{array}{l}CH_2\text{-}SH\\ |\\ CH\text{-}SH\\ |\\ CH_2\text{-}OH\end{array} + \begin{array}{l}Cl\\ \\ Cl\end{array}\!\!>As\,CH = CH\,Cl \rightarrow \begin{array}{l}CH_2\text{-}S\\ |\\ CH\text{-}S\\ |\\ CH_2\text{-}OH\end{array}\!\!>As\,CH = CHCl + 2HCl$$

(BAL) (Lewisite)

HAZARD OF ARSENIC FOR BENEFICIAL INSECTS

1) Vs. Apis mellifera, honey-bee:
   - a) Arsenic is extremely toxic to bees; as As_2O_3 the MLD is 0.2-0.5 μg/bee. 296,2192,2541
   - b) In apple orchards, Pb arsenate is not applied until flower petal fall, at which time the bee-hives are sealed.
   - c) Arsenic is fatal not only to the field worker bees but via the nectar and pollen kills or decimates the colony entire.

d) The chemical sense of bees does not, evidently, detect arsenic-sprayed plants.
e) Death of bees may begin within 3 hours of exposure to Pb arsenate in open, nectar-secreting flowers.
f) Bees caged on Pb arsenate sprayed trees showed 69% mortality; on dusted trees 49% mortality with mortality of caged controls being 19% in the same period of time.
g) Calcium arsenate is intensely hazardous for honey-bees. 907,906,911,2540,2808

2) Toxicity via oral route of arsenic and fluorine compounds for Apis mellifera: 1852,231,290

Arsenicals (as As element)	LD_{50} (μg/bee)	Fluorine Compounds (as F element)	LD_{50} (μg/bee)
Sodium arsenate	1.8	Sodium fluoride	6.0
Calcium arsenate	.7	Sodium silicofluoride	24.0
Acid lead arsenate	5.0	Cryolite	4.2

a) Calcium arsenate in coarse particles, (diameter 18-28 μ) is much less toxic than in fine particles (2-3 μ). 231
b) Acid lead arsenate (particle diameter average: 28μ) may show an LD_{50} dosage up to 185 μg/bee. 231

8

ARSENIC TRIOXIDE (“Arsenic”; White arsenic; Arsenious oxide; Arsenious acid anhydride; Arsenic sesquioxide.)

As_2O_3 Molecular weight 197.82

GENERAL

2815
White arsenic, as arsenic trioxide is commonly known, is the usual source of arsenic for commercial arsenicals 353
used as insecticides. Like other arsenic-containing insecticides, arsenic trioxide is employed chiefly as a 2407
stomach poison for insects in baits and traps. Under proper conditions, arsenic trioxide shows a potent contact 2221
action in insects. The compound is intensely poisonous for animals and plants and presents a high hazard. 1059

PHYSICAL, CHEMICAL

A white amorphous solid or a crystalline powder; the amorphous masses may be glassy; m.p. (octahedral crystals) 275°C, (monoclinic crystals) 313°-315°C; b.p. (sublimes above 150°C, the crystalline forms sublime unchanged, and without fusion, when rapidly heated; amorphous forms fuse before subliming;) d 3.71; v.p. 66.1 mm Hg$^{312°}$; soluble in water to 1.7 parts/100 at 16°C, 10.4 parts/100 at 100°C; solubility is ordinarily given as 2%-4% in distilled water at room temperatures; solution in pure water is slow but in dilute acids and bases rather rapid; soluble in dilute acids, alkalis, carbonate solutions; practically insoluble in organic solvents such as alcohol, chloroform, ether; in water solution becomes arsenious acid (sensu stricto), H_3AsO_3, which by combining with bases yields salts—arsenites; arsenic acid is formed from arsenious acid by the action of fairly strong oxidants; odorless, tasteless (properties which enhance the toxic hazard for animals).

1) Arsenic trioxide equivalents of some common, commercial arsenic insecticides:

Insecticide	As_2O_3 Equivalent Lbs/100 lbs	Insecticide Equivalent Lbs/100 lbs As_2O_3
Lead arsenate	28.5	350.9
Calcium arsenate	36.2	276.2
Paris green	56.8	176.1
London purple	36.2	276.2

TOXICOLOGICAL

1) Toxicity for higher animals:
a) Solutions when ingested are more toxic than the solid compound. 2791,2921

Animal	Route	Dose	Dosage	Remarks	
Man	or	MLD (?)	130 mg/man		2815
Man	or	Toxic	100 mg/man		2221
Man	or	Toxic	0.4-10 ppm	In water.	2954
Mouse	sc	LD	11-13 mg/k		1477

a) Solutions when ingested are more toxic than the solid compound. (Continued) 2791,2921

Animal	Route	Dose	Dosage	Remarks	
Rat (Albino)	sc	LD	8 mg/k		1372
Rat (Norway)	or	LD_{50}	138 ± 13 mg/k		790
Guinea Pig	or	LD	20-39 mg/k	As the sodium salt.	288
Guinea Pig	sc	LD	13 mg/k		447
Guinea Pig	ip	LD	16 mg/k		1477
Rabbit	or	LD	14 mg/k		1676
Rabbit	or	LD	14-30 mg/k	As the sodium salt.	1477
Rabbit	or	LD_{50}	20 mg/k		1870
Rabbit	sc	LD	7-10 mg/k		1477
Rabbit	iv	LD	6 mg/k	Death in 7-20 hours.	1703
Cat	sc	LD	4.7 mg/k		1477
Dog	or	LD_{50}	85 mg/k		1870
Dog	or	LD	30-70 mg/k		1477
Dog	sc	LD	6 mg/k		1477
Dog	iv	LD	3-5 mg/k		1477
Pig	or	MLD	500 mg/animal		2593
Sheep	or	MLD	850 mg/animal		2593
Horse	or	MLD	2000 mg/animal		2593
Cow	or	MLD	2000 mg/animal		2593
Fish	Medium	Toxic	10 ppm		3231
Bass	Medium	Toxic	10 ppm	10 days exposure.	564
Fish	Medium	Harmless	1 ppm		353
Fish	Medium	Harmless	2-7 ppm	1-7 days exposure.	2400
Fish	Medium	Harmless	5 ppm		2400
Fish	Medium	Harmless	7 ppm	1-7 days exposure.	92,386,939
Trout	Medium	Harmless	10 ppm	1 month exposure.	2271
Minnows	Medium	Harmless	17.1 ppm	17.1 hour exposure.	2400
Mussels	Medium	Toxic	16 ppm	3-16 days exposure.	939
Mussels	Medium	Harmless	8 ppm		939
Planaria	Medium	Toxic	40 ppm		939,2400
Fish Food Organisms	Medium	Toxic	2-4 ppm	Includes aquatic insects, etc.	564,939,3021
Zoöplankton (some)	Medium	Harmless	5 ppm		2716

2) Chronic toxicity for higher animals:

- a) Not, strictly speaking, a cumulative poison save in high chronic intake. 353
  - (1) 1-6 weeks required for complete excretion, chiefly via urine and feces. 353
  - (2) More arsenic is deposited in the tissues when calcium arsenate is given than when arsenic trioxide is fed. Marked species variation noted in storing capacity; for example, dog stores much less than rat. 446
  - (3) Normally eliminated much faster than lead, a truly cumulative agent. 2815
  - (4) Sheep tolerated 500 mg/day, cattle and horses 2000 mg/day without symptoms. 2593
  - (5) Development of tolerance ("arsenic fastness") is claimed for human "arsenic eaters." Failure of As_2O_3 to kill in these cases is probably attributable more to the coarse form in which the compound is taken than to any particularly marked tolerance. Fatalities do occur among "arsenic eaters." 2815 1400
  - (6) The importance of the form in which As_2O_3 is taken is illustrated as follows: 2815,1400

    LD, oral, in solution for rats = 75 mg/k or less.
    LD, oral, undissolved, particles 2.5-12.5 μ = ca 100 mg/k.
    LD, oral, crystals, particles of much coarser grain = as much as 500 mg/k.

3) Pharmacological, pharmacodynamic, physiological, etc., in higher animals. (Also consult the section titled, Arsenic and Arsenicals, General Treatment):

- a) Symptoms of intoxication (Man):
  - (1) As_2O_3 is a severe gastrointestinal irritant. In man, within 1 hour of intake: Constricted feeling at throat, sharp, severe stomach pain followed by continued vomiting, diarrhoea, excess urination, with blood present in all effluvia; skin cold and pale, respiration and blood pressure depressed, coma followed by death within the day. 2221 353
  - (2) Chronic effects in man include: Diarrhoea, skin pigmentation, dermatitis, keratosis of palms and soles, puffy oedema of face and limbs, paralysis of limbs (sometimes), mental apathy approaching imbecility, convulsions. 2221 353
  - (3) Arsenic trioxide is known to induce skin cancers. 3225
- b) Symptoms of intoxication (Livestock):
  - (1) In acute poisoning: Stomach ulceration, necrosis. Profound general depression passing over to coma; a characteristic facies is notable, particularly among horses. Calves show a progressive paralysis beginning in the hind-legs and advancing forward, increased respiration, convulsions and death in tetanic spasm. 2593 2404
- c) As_2O_3 is a general protoplasmic poison of protean action and effect, toxic to all plant or animal cells of whatever type. The ultimate action site is probably the systems of cell respiration. 151
  - (1) As_2O_3 brings a specific, irreversible inhibition of respiration in the cell. 2412,3224

(2) Evidence of a profound action on cell systems is afforded by the carcinogenic properties of As_2O_3. This is manifested, in the opinion of some, by the uncoupling of the respiratory and fermentative activities of protoplasm with a consequent irreparable damage to aerobic respiratory systems. 3225

(3) Combines with free SH groups of the dehydrogenases (arsenate does not) as trivalent As. SH-rich substances (cysteine, glutathione, etc.) exert a protective action. 3192 3193

(4) Pentavalent As probably must be reduced to As^{+++} before manifesting toxic effect in the body. 2815

4) Phytotoxicity:

a) Intensely phytotoxic and sometimes used as an herbicide and weed-killer. At concentrations of 1 ppm As_2O_3 blackens the vascular bundles of leaves and kills leaf tissue by chlorophyll poisoning. Bean and cucumber plants are particularly sensitive; turnips, cereals and other grasses are relatively tolerant. In practice, however, As_2O_3 is not applied directly to plants for insect control. Still, the phytotoxicity of other arsenic-containing insecticides is chiefly due to the release, under certain conditions, of soluble As_2O_3 in the form of arsenious acid. Old orchard soils which from arsenical spraying have built up 4-12 ppm of As_2O_3 in the upper layer (particularly in sandy, humus-poor soils) become very unproductive. As_2O_3, per se, presents a marked soil accumulation hazard. Certain plants may concentrate high amounts of As_2O_3; for example, Pentia incana can concentrate as much as 355 ppm in the parts of the plant above ground. 353

5) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Apis mellifera, adult	or	LD	0.76 μg/bee	0.5μg/bee as As perse.	586
Bombyx mori, 4th instar	or	LD_{50}	0.015-0.02 mg/g	Leaf sandwich.*	
Chironomus, larva	Medium	LC	1.96 ppm		
Chironomus, larva	Medium	Tolerated	1.9 ppm		
Mayfly, nymph	Medium	Tolerated	3-14 ppm		
Insects (aquatic), larvae	Medium	Tolerated	10-20 ppm		
Melanoplus bivittatus, adult	or	LD_{50}	0.026 mg/g	In bait. At 0.4 mg/g ST**=33 hrs.	
M. femur-rubrum, adult	or	LD_{50}	ca 0.036 mg/g	In bait.	
M. femur-rubrum	or	LD_{50}	0.137 mg/g	In bait.	
M. differentialis, adult	or	LD_{50}	0.09 mg/g	In bait.	
M. differentialis, adult	or	LD_{50}	0.11 mg/g	In bait.	
Musca domestica, adult	or	LD_{50}	0.18 mg/g	Sirup; as As^{+++}0.14 mg/g.	

*As_2O_5 LD_{50} = 0.02-0.04 mg/g.
**ST = Survival Time.

a) As_2O_3 vs. Musca domestica adults, 1 day after emergence from pupae: 2463

Zone	Number	Body Weight (mg)		Survival Time (hrs)		Dosage (μg/g)		LD_{50} (μg/g)
		M*	R**	M	R	M	R	
Lethal	7	14.4	(13-15)	11	(1-36)	325	(307-349)	
Intermediate	21	14.2	(13-17)	10	(1-15)	220	(109-280)	
"	16	15.4	(13-19.3)	26	(16-50)	228	(152-298)	180***
"	7	14.0	(13-17)	103	(51-144)	197	(181-217)	
"	52	15.3	(13-20)	Survived		186	(111-302)	
Sub-lethal	6	16.5	(15-19)	Survived		95	(95-105)	

*Mean; **Range; ***as As^{+++}= 140 μg/g.

b) Vs. Melanoplus differentialis: 2617

Zone	Number	Survival Time (hrs)		Dosage (μg/g)	LD_{50}(μg/g)
Lethal	22	56	(32-84)	150-440	
Intermediate	17*	80	(22-144)	100†	110
"	14**	–	–	80††	
Sub-lethal	4	Survived		20-40	

*Died; **Survived; †Mean Lethal Dose; ††Mean Recovery Dose.

c) Relative toxicity of pure arsenic oxides. Administered on foliage of appropriate food plants sprayed with solutions or suspensions made to contain 0.076g of the respective oxides per 100cc distilled water. For grasshoppers administered in bran mash baits: 586

Insect	Oxide	Mortality (%) In			
		3 days	6 days	10 days	20 days
Bombyx mori (larva)	As_2O_3	40	58	70	86
" " "	As_2O_5	100	–	–	–
Control, unfed	–	12.2	61.2	71.5	100
Control, fed	–	0	0	0	0
Hyphantria cunea (larva)	As_2O_3	21.6	67.3	95.6	100
" " "	As_2O_5	23.1	77.6	94.2	100

c) Relative toxicity of pure arsenic oxides. Administered on foliage of appropriate food plants sprayed with solutions or suspensions made to contain 0.076g of the respective oxides per 100cc distilled water. For grasshoppers administered in bran mash baits: (Continued) 586

Insect	Oxide	Mortality (%) In			
		3 days	6 days	10 days	20 days
Control, unfed	—	0	28.7	93.6	100
Control, fed	—	0	0.6	4.1	21
Malacosoma americana (larva)	As_2O_3	4.6	50.5	78.9	100
" " "	As_2O_5	62.1	85.2	87.6	100
Control, unfed	—	0.4	15.3	79.3	100
Control, fed	—	1.9	5.5	12.3	50.5
Leptinotarsa decemlineata (adult)	As_2O_3	19.2	23.1	—	35.1
" " "	As_2O_5	65.1	65.0	—	100
Control, unfed	—	—	—	—	—
Control, fed	—	14.6	20.7	—	57.1

(1) Average mortality (%) all species before deducting control mortality:
As_2O_3 = 94.6%
As_2O_5 = 100 %
(2) Average toxicity: As_2O_3 = 46.1%; As_2O_5 = 76.5%.

d) Amount of water-soluble arsenic and toxicity. As_2O_3 and As_2O_5 given as solutions or suspensions made to contain 0.076g oxide per 100cc; grouped data gathered in tests vs. Bombyx mori, Hyphantria cunea, Malacosoma americana, Leptinotarsa decemlineata: 586

Compound	Water-Soluble As (%)	Net Toxicity (%)
As_2O_3	17.8	46.1
As_2O_5	100	76.5

e) Vs. Melanoplus adults; comparative toxicities by oral administration of toxicants in baits: 2611

Compound	LD_{50} (μg/g) For		
	M. bivittatus	M. femur-rubrum	M. differentialis
Arsenic trioxide	26*	360 (ca.)	90
Sodium arsenite	15**	100	—
Sodium fluosilicate	100***	120	—
Sodium fluoride	40 (ca.)	—	110

*Survival Time at 40μg/g = 33 hours.
** " " " " " " = 20 " .
*** " " " " " " = 33 " .

f) Used vs. grubs of Popillia japonica in the soil, As_2O_3 yielded greatly variable results, acting in this respect no differently than other arsenicals such as arsenates of aluminum, di- and tri-calcium, manganese. 1026

6) Pharmacological, pharmacodynamic, physiological, etc., insects:

a) The following histopathological signs may be noted in larvae of Prodenia eridania a few hours after poisoning but prior to death: Epithelial cell destruction in gut with cell disintegration, loosening of epithelium from basement membrane, cytolysis, cytoplasmic vacuolization, clumping, dispersion or dissolution of nuclear chromatin, disintegration of the striated border, breakdown of the cell membrane. 3349

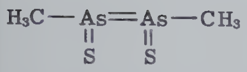
b) In Blatta, after oral poisoning by As_2O_3, a marked reduction in haemocytes has been noted. The reduction ranged from counts of 35,000 per cc down to 7000 per cc, with the disappearance of the larger cell types. Similar effects occurred in Locusta. 1007 2511

c) In Leptinotarsa decemlineata As_2O_3 caused a marked decline in respiratory rate. 997

d) In Periplaneta americana a cathartic effect, markedly reducing the food passage time through the gut, was observed. 2917

9

ARSENOMETHANE DISULFIDE (Arsenomethane As-1, 2-disulfide; Compound A-42)



$$H_3C-\underset{\underset{S}{\|}}{As}=\underset{\underset{S}{\|}}{As}-CH_3$$

Molecular weight 244.01

GENERAL

A substance which has shown insecticidal promise, being highly toxic for Tribolium confusum, Blattella germanica, and certain other insects. 2635

CHEMICAL, PHYSICAL:

1) Synthesis:
   a) Methylation of sodium arsenite → disodium methylarsonate.
   b) Reduction - sulfurization of disodium methylarsonate by sodium sulfite, sodium thiosulfate, hydrochloric acid, → arsenomethane disulfide.

2) A solid; m.p. 93°C; b.p. (with decomposition) 250°-260°C; $d_{4°}^{25.3°}$ 1.14; v.p. 0.0006 mmHg$^{27°}$, 0.005 mmHg$^{50°}$, 0.02 mmHg$^{80°}$; volatility: 0.14% evaporation in one week under atmospheric conditions; solubility: in water, 1g/500cc (distilled water) in 24 hr, very soluble in CS_2, somewhat soluble in naphtha, chloroform, ethyl ether, slightly soluble in kerosene, ethanol, methanol, methylated naphthalenes, insoluble in xylene, toluene, petroleum ether, benzene; water soluble arsenic = 4.8% of total arsenic; properties are generally acidic, salt-forming; tendency to dimerize; incompatible with strong bases, cationic surface active agents; keto-, aldehyde, carboxylic, and carbonyl compounds impair insecticidal action.

3) Formulations:
   a) As dusts (with which the best results are obtained); as water wettable powders; for example, arsenomethane disulfide 50% by weight + Ca $(OH)_2$ 48% by weight + "Daxad # 21" 1% by weight + Duponol WA powder 1% by weight.

TOXICOLOGICAL

1) Toxicity for man and higher animals apparently corresponds to the general range established for inorganic arsenical insecticides. No quantitative toxicological data are available for laboratory animals.

2) Phytotoxicity:
   a) Maximum concentrations which have been used without plant injury: 2635

	Sprays			Dusts	
Plant	Concentration (lb/gal)	$Ca(OH)_2$ (corrective)	Applications (no.)	Concentration (%)	Applications (no.)
Potato	0.5	—	1	1 % in Attaclay	1
Tomato	0.25	—	1	1 % in Attaclay	2
Tomato	—	—	—	5% in Attaclay	1
Pepper	0.25	—	2	10% in $Ca(OH)_2$	1
Cucumber	0.25	—	1	—	—
Corn	0.25	1	1	—	—
Bean	—	—	—	0.5% in Attaclay	1
Peach	0.01	—	1	3.0% in $Ca(OH)_2$	1
Peach	0.1	0.2	1	—	—
Peach	0.025	—	1	—	—
Pear	0.25	1	1	1% in Attaclay	3
Pear	0.025	—	1	1% in Attaclay	1
Apple	0.075	—	1	0.5% in Attaclay	2
Apple	0.25	—	1	—	—

   b) Minimum concentrations yielding plant injury:

Potato	0.75	—	1	3.0% in Attaclay	1
Tomato	0.25	—	3	1.0% in Attaclay	3
Tomato	1.0	4.0	1	10.0% in Attaclay	1
Pepper	0.5	—	3	—	—
Pepper	1.0	4.0	1	—	—
Cucumber	0.5	—	1	1.0% in Attaclay	1

b) Minimum concentrations yielding plant injury:

Plant	Sprays			Dusts	
	Concentration (lb/gal)	$Ca(OH)_2$ (corrective)	Applications (no.)	Concentration (%)	Application (no.)
Corn	0.05	—	1	0.5% in Attaclay	1
Corn	0.25	0.5	1	1.0% in $Ca(OH)_2$	1
Bean	0.075	—	1	0.8% in Attaclay	1
Bean	0.05	—	1	—	—
Pear	0.075	—	1	—	—
Pear	0.25	0.5	1	—	—
Apple	0.075	—	2	0.5% in Attaclay	3
Apple	0.25	1.0	1	5.0% in Attaclay	1

(1) Phytotoxicity, in inert carriers, is near or beyond the margin of safety. The danger of injury to plants is reduced by correctives, for example, hydrated (slaked) lime.

c) Arsenomethane As-1, 2-disulfide, and others, toxicity for cotton seedlings growing in a hydroponic medium: 894

Compound	% Seedlings Damaged Beyond Recovery At Concentrations Of				
	1: 100	1: 1000	1: 10,000	1: 100,000	1: 1,000,000
Arsenomethane As-1,2-disulfide	100	70	12	10	0
Copper aceto-arsenite	100	100	100	38.47	9.1
Tricalcium arsenate	58.85	76.93	9.1	7.7	0
Acid Lead arsenate	100	100	33.3	0	0
DDT	0	0	0	0	0
Chloroarsenomethane As-1,2-disulfide	100	100	100	0	0
Control seedlings mortality %	0	0	0	0	0

3) Toxicity for Insects:

a) LD_{50} dosages of arsenomethane disulfide compared with LD_{50} dosages of some other insecticides: 2635

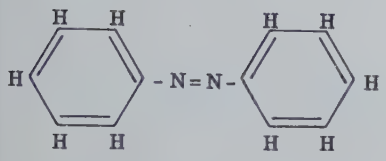
Insecticide	LD_{50} (concentration %) For			
	Tribolium confusum	Epilachna varivestis	Blattella germanica	Leptinotarsa decemlineata
Calcium arsenate	2.0	5.0	2.5	4.0
Rotenone	0.25	0.15	0.5	0.25
DDT	0.015	—	2.0	2.5
Parathion	0.0005	—	—	—
Arsenomethane disulfide (crude)	0.015	2.0-4.0	0.25	1.0
" " (pure)	0.005	—	—	—

b) Toxicity of arsenomethane disulfide for various insects: 2635

Insect	LD_{50} (approximate)	On	Remarks
Tribolium confusum	0.005% in medium	wheat flour	—
Termite (sp?)	0.05% in medium	soil, sawdust	—
Sitophilus granarius	0.1% in medium	whole grain	—
Attagenus piceus	(1.0% mortality after 30 day)	soy-wheat flour	—
Grasshopper (sp?)	0.5 lb/gal spray → LD_{90}	grass	—
Grasshopper (sp?)	4.0% in poison bran	grass	—
Grasshopper (sp?)	5.0% dust in $Ca(OH)_2$	grass	Grass slightly "burned."
Popillia japonica	5.0% dust in $Ca(OH)_2$	smartweed	—
Epilachna varivestis	2-4% dust in $Ca(OH)_2$	bean plants	Severe injury to plants.
Leptinotarsa decemlineata	5.0% dust in $Ca(OH)_2$	potato plants	Severe injury to plants.

10

AZOBENZENE (Azobenzide; Diphenyl diimide; Azobenzol; Benzene-azobenzene)



Molecular weight 182.22

GENERAL: [Refs. 1001,1000,257,1394]

An insecticidal and acaricidal compound of rather highly specific action. Primarily employed as an acaricide and having its greatest value as a thermal "smoke," or low vapor pressure fumigant, to control two-spotted red spider mites, Tetranychus bimaculatus, on greenhouse plants.

PHYSICAL, CHEMICAL: [Refs. 2221,2231,353,900,2815]

Orange-red dyestuff; a crystalline solid; m.p. 68°C; b.p. 293°C [Ref. 2221], 297°C [Ref. 2231]; $d_{4°}^{20°}$ 1.203; v.p. 4 x 10^{-3} mmHg$^{25°}$; appreciably volatile; sublimes at temperatures much below the boiling point; insoluble in water; soluble in most organic solvents, for example alcohols, ether, glacial acetic acid; odor is sweetish and not unpleasant; stable, under ordinary conditions. Replacement of the azo bridge, -N=N-, by — CH_2OCO- , as in benzyl benzoate, q.v., or by -SO_2, as in diphenyl sulfone and p-chlorophenylphenyl sulfone, q.v., does not markedly reduce the acaricidal properties. Smoke, deposited as minute drops on surfaces is stable at 20°C, although the setting point is 60°C. 2807

Formulations:

- a) As water pastes with 70% azobenzene in diatomaceous earth to be applied to hot water pipes and volatilized as a greenhouse fumigant.
- b) In mixtures, with 40% azobenzene, to be ignited for production of thermal "smoke" in greenhouses, under tents, etc.
- c) As dusts, wettable powders, and miscible concentrates for spray preparation.

TOXICOLOGICAL:

1) General:
- a) Toxic to rats if fed or injected in considerable quantity. 258
- b) The vapor, as used in greenhouse fumigation, is not considered particularly dangerous. A felt-pad respirator is deemed a sufficient precaution. 258

2) Phytotoxicity:
- a) Not generally considered hazardous to plants when used at acaricidal concentrations. Roses and asparagus fern are subject to damage. 2120
  - (1) Rose flowers, produced from buds present at time of treatment, fade badly and must be discarded. 2870
    2867,34
  - (2) Saintpaulia (African violet) is highly susceptible to damage. 353
  - (3) Phytotoxic to apple trees; 0.1% sprays defoliated the tree leaving the fruit on branches. 947,1512
  - (4) Used in the field at 0.05%, azobenzene has caused leaf-fall of apple trees; at 0.1% severe fruit fall has occurred; at 0.03% considerable pest control of Metatetranychus ulmi on apples may be had with only slight damage to foliage. 1808 900
- b) Less danger of plant injury to roses if used as a dust, which is tolerated at higher temperatures than the fumigant vapor or smoke. 1357

3) Toxicity to Insects and Acarina:
- a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Mosquitoes (culicine) (larvae)	Medium	LC_{50} or >	5 ppm	Exposure 16 hours; larvae 4th instar.	1001
Periplaneta americana (adult) ♂	Topical	LD_{50}	0.8 mg/g	Average weight insect = 0.9g(0.7-1.15g).	2219
Periplaneta americana (adult) ♀	Topical	LD_{50}	1.3 mg/g	Average weight insect = 1.3g(1.0-1.9g).	2219
Periplaneta americana (adult) ♂	Topical	LD_{100}	1.1 mg/g	Average weight insect = 0.9g(0.7-1.15g).	2219
Periplaneta americana (adult) ♀	Topical	LD_{100}	2.0 mg/g	Average weight insect = 1.3g(1.0-1.9g).	2219
Periplaneta americana (adult) ♂	Topical	LD_0	0.5 mg/g		2219
Periplaneta americana (adult) ♀	Topical	LD_0	0.85 mg/g		2219
Periplaneta americana (adult) ♂	inj	LD_{50}	0.43 mg/g	Average weight insect = 0.9g(0.7-1.15g).	2219

3) Toxicity to Insects and Acarina:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Periplaneta americana (adult) ♀	inj	LD_{50}	0.62 mg/g	Average weight insect = 1.3g(1.0-1.9g).	2219
Periplaneta americana (adult) ♂	inj	LD_{100}	0.57 mg/g	Average weight insect = 0.9g(0.7-1.15g).	2219
Periplaneta americana (adult) ♀	inj	LD_{100}	0.82 mg/g	Average weight insect = 1.3g(1.0-1.9g).	2219
Periplaneta americana (adult) ♂	inj	LD_0	0.32 mg/g		2219
Periplaneta americana (adult) ♀	inj	LD_0	0.5 mg/g		2219

b) Action of 10% azobenzene dusts in bentonite against several crop insects: 1394

Insect	Exposure (days)	% Mortality	
		Experimental	Control
Leptinotarsa decemlineata (adult)	7	100	0
Epilachna varivestis (larva)	5	100	0
Epilachna varivestis (adult)	3	100	0
Malacosoma americana (larva)	2	90	0

c) Action of azobenzene + whiting dusts on *Tetranychus bimaculatus*: 1394

Concentration (%)	Mortality In 48 hr (%)
20	100
5	100
2	95.4
1	94.3
0.5	80.8

4) Azobenzene in the economic control of insects and Acarina:

a) Ineffective, in the field, vs. *Epilachna varivestis*, although it has been used against this insect. 353,918

b) Effectively controls mosquitoes as a larvicide at 1 part in 200,000 parts water. 1001

c) Used as a greenhouse thermal fumigant (70% azobenzene + 30% inert paste in diatomaceous earth) gave 90-99.75% kill of all stages (including eggs) of *Tetranychus bimaculatus*; dosage = 1 lb mixture/40,000 ft^2. 1394

d) Outstanding in the control of *Tetranychus bimaculatus* on Lima beans. 1619

e) Effectively controlled *Brevipalpus spp.*, which resist parathion. 1357

f) As a dust at 25%, thoroughly applied, effectively controls most spider mites on roses; a 50% dust is preferable if the unsightliness of inert residues on plants must be avoided. 1357

g) Effective in control of *Tetranychus bimaculatus*, *Paratetranychus ilicis*, *Brevipalpus spp.*, "broad mites." 1357

h) Highly toxic, in laboratory experiments as a 0.1% spray, for the summer eggs of *Metatetranychus ulmi*. The same concentration yielded 75% mortality of adult females. In the field, an 0.03% spray on apples, yielded considerable control of *M. ulmi* without (or with slight) damage to foliage. 1808

5) Other azo-compounds, both more toxic and less toxic for culicine mosquito larvae than azobenzene: 1001

a) Compounds more toxic than azobenzene (LC_{50} 16 hr = 5 ppm) for culicine larvae:

Compound	LC_{50} (or more) 16 hrs (ppm)
4-(p-Bromophenylazo)-o-cresol	1.42
4-(p-Bromophenylazo)-resorcinol	1.42
4-(p-Bromophenylazo)-m-cresol	1.66
p-Bromophenyl azophenol	1.66
4-(2,5-Dichlorophenylazo)-o-cresol	1.66
4-(2,5-Dichlorophenylazo)-m-cresol	2.5
4-(2,5-Dichlorophenylazo)-resorcinol	2.5
4-(p-Iodolphenylazo)-o-cresol	2.5
1-Phenylazo-2-naphthylamine	3.3
4-(p-Nitrophenylazo)-resorcinol	3.3

b) Compounds as toxic as azobenzene:

Compound	LC_{50} (or more) 16 hrs (ppm)
4-(p-Bromophenylazo)-5,6,7,8-tetrahydro-1-naphthol	5.0
1-(p-Bromophenylazo)-2-naphthylamine	5.0
p-(2,5-Dichlorophenylazo)-o-cyclohexylphenol	5.0
p-(2,5-Dichlorophenylazo)-phenol	5.0

c) Compounds less toxic than azobenzene (LC_{50} 16 hr = 10-100 ppm):

(1) Phenylazo-o-cresol
(2) Phenylazo-m-cresol
(3) p-Phenylazoaniline
(4) p-Phenylazophenol
(5) 1-(o-Tolylazo)-2-naphthylamine
(6) 4-(2,5-Dichlorophenylazo)-3-ethoxyphenol
(7) 4-(2,5-Dichlorophenylazo)-2,5-xylenol
(8) p-Phenylazo-dimethylaniline
(9) p-Phenylazo-diphenylamine
(10) p-Iodobenzene

6) Azoxybenzene, $C_6H_5\overset{\overset{O}{\uparrow}}{N}{=}N{-}C_6H_5$, a close relative of azobenzene, is also toxic to insects, being effective against the European corn-borer, and superior in effectiveness against the larvae of Cochliomyia americana. 406 2563

7) Screening tests. 1801
   - a) Highly rated as an insecticide for lice; some ovicidal activity.
   - b) Highly rated as a mosquito larvicide.
   - c) Good rating in "KD" capacity for fleas; some ovicidal activity.
   - d) Superior rating, at least = to DDT as a tick toxicant; high rating for "KD" activity vs. ticks.
   - e) Good rating for "KD" activity vs. chiggers; some killing activity.
   - f) High rating for repellency vs. Aëdes aegypti
   - g) High rating for residual activity vs. A. aegypti; some activity vs. Musca.

8) Specificity of action:
   - a) Used in greenhouses as a dust (20% azobenzene + 80% whiting) to control red spider on carnation plants, azobenzene showed little effect on Phlyctaenia rubigallis, the greenhouse leaf tier, or on several species of Aphids. 2815

9) Pharmacological, physiological and biological; insects:
   - a) Neurotoxic. 353
     - (1) Yielded a marked and immediate rise in O_2 consumption in the poisoned insect.

11

BARIUM SILICOFLUORIDE (Barium fluosilicate)

$BaSiF_6$ Molecular weight 279.42.

GENERAL [Refs. 1940,2120,2106,2815,353,2221]

Introduced experimentally as an insecticide in 1926, but now of declining interest in insect control. As an insecticide it may be classed in same general order of activity and usefulness as acid lead arsenate. Has the same high phytotoxic potential of other silicofluorides, and is very poisonous to man and animals. Recommended, in Europe, as a substitute for hazardous zinc phosphide in mole cricket control. For most purposes cryolite, rotenone and chlorinated hydrocarbons are displacing this substance. Has an advantage over sodium silicofluoride in that, being much less soluble, it may be used as a dust or suspension on tolerant growing plants.

PHYSICAL, CHEMICAL [Refs. 2221,353,2815,129]

White crystalline powder; odorless; highly poisonous and easy to mistake for other substances of common household use; d 4.3; slightly soluble in water, 0.03% at 21°C, 1 part in 4000 of cold water, 1 part in 1110 parts water at 100°C, the resulting solution being acid in reaction; decomposed by alkalis; incompatible with lime sulfur, Bordeaux mixture, nicotine sulfate, and other soluble sulfates, with which it yields barium sulfate and phytotoxic soluble silicofluorides; corrosive to metals (the commercial product contains 8% cryolite to protect containers and metal sprayers).

Formulations:
- a) As a powder or dust, for example 1:3 in talc, for Epilachna varivestis and various flea and blister beetles.
- b) As "Dutox," 72% barium silicofluoride + 8% cryolite.
- c) Baits; sprays at 4 lbs/100 gallons water. 96

TOXICOLOGICAL

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}ca	175	As a suspension in water.	1951
Rabbit	or	MLD	175		2312
Chicken	or	LD	100		1750
Pigeon	or	LD	170		1750

  a) Toxicity depends on the amount of fluoride ion in solution. Toxicity is enhanced by any circumstance 353
  which brings the compound into solution. 129
  b) Poisonous to man, domestic animals and wild life, but less toxic than sodium fluoride because of relative 353
  insolubility. 129

2) Chronic toxicity:
  a) Chronic intoxication with fluorine compounds, depending on severity, may produce such signs and symptoms as tooth mottling, anorexia, general cachexia with bone fragility, stiffness of hands and signs of respiratory paralysis. 545
  b) 0.0904% F in food, daily, from fluorides, fluosilicates (including Ba fluosilicate) brings death in 9-11 days. 2888

3) Hazard:
  a) Residues: Apples from trees sprayed with barium silicofluoride show average residues, before scrubbing, of 5.6 ppm. 2815
    (1) Tolerance limit for fluoride on apples (1938) is 2.8 ppm.
  b) A principal hazard is mistaken ingestion of roach powders containing barium silicofluoride when confused 353
  with food products. Coloring of such powders, as a warning, is a requirement in some localities. 129

4) Phytotoxicity:
  a) Phytotoxic, but due to insolubility, may be used on plants with proper precautions. 2371
  b) Injurious to foliage and fruit of peach tree. 2106
  c) May, at moderate doses, "burn" grape foliage and shoots. 258
  d) Harmless, at 1500 lbs/acre, to blue grasses, sensitive to equivalent dosages of lead arsenate. 2027

5) Toxicity for Insects:
  a)

Insect	Route	Dose	Dosage	Remarks	
Ascia rapae (5th instar)	or	LD_{50}	0.43 (0.34-0.67) mg/g	Death in 20-48 hr.	944
Bombyx mori (4th instar)	or	LD_{50}	0.09-0.12 mg/g		2819
Bombyx mori (4th instar)	or	LD_{50}	0.17 mg/g	In leaf sandwich.	459

  b) Comparative toxicity and solubility of barium silicofluoride, other fluorine-containing compounds, and acid lead arsenate: 2819
    (1) Test insect: *Bombyx mori* (4th instar); oral route.

Compound	Grams Soluble/100cc$H_2O^{25°C}$	LD_{50} (mg/g)
Barium silicofluoride	0.025	0.09-0.12
Sodium fluoride	4.054	0.11-0.15
Lead fluoride	0.066	0.25-0.40
Sodium silicofluoride	0.762	0.10-0.13
Potassium silicofluoride	0.177	0.07-0.10
Sodium fluoaluminate	0.061	0.06
Potassium fluoaluminate	0.158	0.08-0.10
Acid lead arsenate	—	0.086

PHARMCOLOGICAL, BIOLOGICAL; INSECTS

1) See the general treatment titled Fluorine, Fluorides, Silicofluorides.
  a) Primarily a stomach poison, possibly with some contact action. 2815,353
  b) *Prodenia* larvae, poisoned with barium fluosilicate: At first sluggish with occasional convulsive spasms declining until death in flaccid paralysis. 3349
    (1) In contrast to sodium fluoride, sodium silicofluoride poisoning yielded no histopathology in *Prodenia*.

2) Certain strains of *Carpocapsa pomonella* manifest "acquired" resistance to barium silicofluoride. 1602

EFFECTS ON BENEFICIAL INSECT POPULATIONS

1) Used as "Dutox," spray, (barium silicofluoride + sodium fluoaluminate) at 1½ lbs/50 gal water an average kill of 14% (11-18%) of adult *Hippodamia convergens* was noted; larvae: 0-2% kill; eggs: no kill. 1450

USES IN THE ECONOMIC CONTROL OF INSECTS

1) Vs. *Scapteriscus*, *Gryllotalpa*: Effective. 1750
2) Vs. *Protoparce sexta*. (Control with DDT requiring 10 lbs/acre is considered too costly.) 36,37
3) Vs. *Ancylis comptana*, *Leptinotarsa decemlineata*: Effective. 353
4) Vs. *Epicauta* spp: Quick control with 25% dusts at 25 lbs/acre. 353
5) Vs. *Diabrotica melanocephala*, *D. duodecempunctata*: 75% kill; superior to other inorganic dusts. 1233
6) Vs. *Sitona cylindricollis*: 40% control was the maximum achieved. 353
7) *Thermobia domestica* was controlled by 4% baits. 353

12

BEES AND INSECTICIDES: BENEFICIAL INSECTS AND INSECTICIDES: (For a bibliography to 1950 see Ref. 2333)

I) SUMMARY [Refs. 3099,1330,1704,910,429,3098,231,296,927,2815,996,2192,427]

1) Arsenicals:
   - a) All arsenicals, for example, Paris green and calcium arsenate, as used on blooming plants in orchards, cotton fields, alfalfa and clover plantings, etc., are intensely hazardous and harmful to bees. The toxic potential is long lasting, and the effect is carried to the hive itself.

2) Organic and other insecticides:
   - a) Safe for bees, when properly applied to blooming plants:
     - (1) Toxaphene. (Perhaps the least toxic, by mouth and contact, of all the chlorinated hydrocarbons. A 10% dust, on alfalfa in bloom, caused less than 10% mortality in the working honeybee field force.)
     - (2) Phenothiazine. (Almost non-toxic to bees.)
     - (3) Methoxychlor. (Oral toxicity slight; contact toxicity high; residue hazard slightly less than that of DDT.)
     - (4) Sulfur.
     - (5) Ryania. (Only slightly toxic to bees by contact.)
     - (6) Nicotine. (Virtually harmless in the field; oral LD$_{50}$: 50 μg/bee.)
   - b) Safety for bees on flowering plants questionable (conflicting experiences):
     - (1) DDT. (Toxicity affected by particle size; LD$_{50}$, in range of 20°-36°C, = 32-560 μg/bee.)
     - (2) DDD. (Less toxic than most chlorinated hydrocarbons; residual contact hazard.)
     - (3) Chlordane.
   - c) Unsafe, hazardous, for bees on flowering plants:
     - (1) BHC. (100-250 times as toxic as DDT in normal temperature range; highly toxic orally, by contact and by residual action.)
     - (2) Lindane. (γ-BHC; as above.)
     - (3) Aldrin. (Highly toxic orally, by contact, residually and by fumigant action.)
   - d) Very hazardous and destructive to bees on flowering plants:
     - (1) Parathion. (Most toxic of all; 3 times as toxic as pure γ-BHC [lindane].)
     - (2) Dieldrin. (Hazard persists for at least 1 week after application.)
     - (3) HETP. (No residual action; high stomach and contact toxicity.)
     - (4) TEPP. (High stomach and contact toxicity; residues kill for 2 days at least.)
     - (5) Arsenic. (All forms are hazardous.)
     - (6) Derris. (Dust lethal to bees visiting plants in bloom.)
     - (7) Sabadilla. (Highly toxic, but no residual hazard; 100% kill on dusted alfalfa.)
     - (8) Pyrethrum. (Highly toxic by direct contact (0.001% solutions) and orally; 0.01% sprays and 0.02% dusts, however, are considered safe in the field.)
     - (9) Rotenone. (Highly toxic by direct spray contact (0.125%) oral toxicity very high.
     - (10) DNOC, DNCHP. (Exceedingly toxic to bees; rarely, if ever, used on plants in bloom.)
     - (11) Malathion and Diazinon. (Very hazardous to bees on sprayed alfalfa.)
   - e) The organic insecticides which have been tested are generally considered safe for honeybees in flowering fields and orchards 48 hours after application. Dieldrin, however, renders fields hazardous to bees for at least 1 week.
   - f) Systox®, applied after 6 P.M. and before 7 A.M. when bees are not foraging, is apparently absorbed rapidly enough by plants not to be a hazard on alfalfa.
   - g) CS-708 controls pea aphid and in laboratory trials is virtually non-toxic to bees.

3) "Danger Index" of certain insecticides for Apis mellifera: 1330
   - a) $\frac{Ca}{Ct}$ = Danger Index: Where Ca = concentration of insecticide applied in agriculture in % (a measure of the extent of exposure) and Ct = the concentration which contains the absolute LD$_{50}$ in 10 cc of solution.
   - b) The higher the index, the greater is the hazard of the toxicant for honey bees.
   - c) LD$_{50}$ determined by direct feeding of the toxicant via micropipette.

Insecticide	Concentration Used In Practice (%)	LD$_{50}$ (μg/bee) at 28°C	LD$_{50}$ (μg/bee) at 36°C	Danger Index at 28°C	Danger Index at 36°C
DDT* (wettable powder)	0.1	300	560	0.03	0.02
DDT (emulsion)	0.05	10	30	0.5	0.02
BHC (wettable powder)	0.01	0.37	0.2	3	5
Parathion (emulsion)	0.01	0.1	0.09	10	11
Calcium arsenate (wettable)	0.4	5	4	8	10

*LD$_{50}$, in the temperature range from 20°-36°C, = 32-560 μg DDT/bee.

II) TOXICITY OF INSECTICIDES OF VARIOUS CLASSES FOR APIS MELLIFERA (ADULT):

1) Arsenicals: (Bees cannot, apparently, discriminate arsenical-sprayed from unsprayed trees. Minimum lethal dose of arsenicals generalized as 0.2-0.5μg/bee.) 296 2192

Calcium arsenate:

Oral LD_{50} (as the element) 0.7μg/bee (fine-medium); 0.6μg/bee (commercial); 1.3μg/bee (coarse). 1852
Oral LD_{100} (as the element) 0.9μg/bee (fine); 1.0μg/bee (medium); ca2μg/bee (coarse). 231
Oral LD_{50} (wettable powder) 5μg/bee at 28°C; 4μg/bee at 36°C. 1330

Sodium arsenate: 1852

Oral LD_{50} (as the element) 1.8μg/bee.

Acid lead arsenate: 1852

Oral LD_{50} (as the element) 5.0μg/bee. 1852
Oral LD_{100} (as the element) ca15.0μg/bee (fine); ca350μg/bee (coarse) 231

2) Fluorides, fluosilicates, fluoaluminates:

Sodium fluoride:

Oral LD_{50} (as fluorine) 6.0μg/bee. 290

Sodium fluosilicate:

Oral LD_{50} (as fluorine) 24.0μg/bee. 231

Cryolite:

Oral LD_{50} (as fluorine) 4.2μg/bee (fine); 5.5μg/bee (medium); 13μg/bee (coarse). 231
Oral LD_{100} (as fluorine) ca18μg/bee (fine); ca9μg/bee (medium); ca71μg/bee (coarse). 231

3) Chlorinated hydrocarbons:
Aldrin: Oral LD_{50} 0.25μg/bee. 910
DDT: Oral LD_{50} 4.6μg/bee (at room temperatures); 12.0μg/bee at 95°F. 910
DDD: Oral LD_{50} 16.0μg/bee. 910
BHC (γ90%): Oral LD_{50} 0.15μg/bee. 910
Chlordane: Oral LD_{50} 1.2μg/bee. 910
Toxaphene: Oral LD_{50} 22.0μg/bee. 910

4) Organophosphorus compounds:
Hexaethyl pyrophosphate: Oral LD_{50} 0.29μg/bee. 910
Tetraethyl pyrophosphate: Oral LD_{50} 0.75μg/bee. 910
Parathion: Oral LD_{50} 0.07μg/bee (high contact toxicity, strong fumigant effect; hazard = to that of calcium arsenate.) 910,1330 3098

5) Other toxicants:
Nicotine: Oral LD_{50} 50μg/bee (virtually harmless in the field). 231
Pyrethrum: Oral LD_{50} 0.3μg/bee; LC (as contact spray) 0.001% solution. 2815,927
Rotenone: Oral LD_{50} 0.6μg/bee; LC (as contact spray) 0.125% solution. 996

6) % Mortality of Apis mellifera exposed to various doses of arsenicals: 231

Dosage (μg/bee) (as arsenic element)	Average life in days	% Mortality After		
		1 day	2 days	3 days
	Acid lead arsenate			
0.1	8.35	0	3	5
0.8	11.35	0	0	0
1.6	10.84	0	0	2
6	6.56	1	2	18
12	3.79	0	17	41
24	1.39	29	85	97
48	0.91	60	99	100
CONTROL	16.24	0.1	0.4	1.4
	Calcium arsenate			
0.1				1
0.8				88
1.6				100
CONTROL				1.4
	Arsenic pentoxide			
0.1				4
0.8				43
1.6				100
CONTROL				1.4

7) Toxicity of various practical field formulations of chlorinated hydrocarbon insecticides for Apis mellifera: 3248

3% γ-BHC + 5% DDT + 40% sulfur (dust) contact LD$_{50}$ 1.9 lb/acre.
3% γ-BHC + 40% sulfur (dust) contact LD$_{50}$ 2.3 lb/acre.
5% DDT + 82% sulfur (dust) contact LD$_{50}$ 9.6 lb/acre.
10% Chlordane + 40% sulfur (dust) at $<$ 76°F only slightly toxic at 29.95 lb/acre
at 86°F toxicity at 29.95 lb/acre greatly increased.
20% Toxaphene + 40% sulfur (dust) at 36 lb/acre yielded only 5% mortality.

8) Relative toxicity of insecticides for Apis mellifera (adult) based on the LD$_{50}$ and by the most effective route of administration: 206

Toxicant	Most Effective Route	Relative Toxicity
Arsenic	enteral	1
Parathion	enteral, fumigant (?)	17
DDT	parenteral	43
Ethylene dichloride	fumigant	10,435
Nicotine	parenteral	11,304

9) Toxic effects of certain insecticides on Apis mellifera: 910

Toxicant		LD$_{50}$ 72 hrs (μg/bee)	Stomach Poison Time (hrs)	Contact Poison Time (hrs)	Fumigant Action Time (hrs)
BHC (90% γ-isomer)		0.15	3-24	0.1-0.5	0.5-1.5
Chlordane		1.21	5-24	0.1-0.5	1.5
JH-118 (chlordane relative)		0.25	6-144	1-2	4
DDD		16.0	2-72	2	0
DDT	(room temp.)	4.6	1-48	5+	0
	(95°F)	12.0+	5-120	5+	0
HETP		0.29	2-24	1-48	
Parathion		0.07	1-24	0.5	3-6
TEPP		0.75	1-24	0.5	
Toxaphene		22.0	5-24	1-3	0

10) Toxic effects of various insecticides on Apis mellifera: 927

a) Cage tests; contact: Deposits on paper covering 60% cage surface; oral: Insecticide fed in honey-water; spraying, dusting: From a 2-foot distance in closed room; dust 1g/cage; spray 4cc/cage.

Insecticide; Method	% Mortality After 24 hrs	48 hrs	72 hrs	
Cryolite (synthetic), spray	75	75	—	
" " , "	0	40	60	
" " , contact (0.002g/cm^2)	100	—	—	
" " " "	10	25	65	(100% affected at 72 hrs.)
" " , oral 1:800 in 1:1 honey, H$_2$O	65	75	85	
" " , spray 1:400	5	15	25	(100% affected at 72 hrs.)
DDT 50% wettable 1:400, contact	100	—	—	
" 5% dust, 1g at 4 ft	5	15	15	
" .025%, in 1:1 honey + H$_2$O oral	0	100	—	
" 5%, dust 1g at 2 ft	90	95	—	
" acetone sol, .002g/cm^2 spray	100	—	—	
" " " , .001g/cm^2 spray	100	—	—	
" " " , .0004g/cm^2 spray	100	—	—	
" wett. pwdr. .0625% 1:800 in 1:1 honey + H$_2$O oral	30	100	—	
" " " , 1:400, .01g/50cm^2 contact	100	—	—	
" " " , 1:400 spray 4cc at 2 ft	20	35	50	

b) Pyrethrins: (An extract containing 0.69% pyrethrins) + piperonyl cyclohexenone 6.92% (referred to hereafter as "extract")

c) Dust: Piperonyl cyclohexenone 5% + pyrethrins 0.004% (referred to as "dust")

Insecticide; Method	% Mortality After 24 hrs	48 hrs	72 hrs	
Extract 1:600, spray 1cc/50cm^2 (0.0023 mg/cm^2) dried 12 hr, contact	0	0	0	
Dust, 1g at 2 ft	0	0	0	Bees irritated.
Extract, 1:1200 in honey-H$_2$O 1:1	0	20	20	Bees repelled.
Dust, 1g at 1 ft	15	15	15	KD 100% in 30 min.
Extract, 1:400 (0.25%) spray 4cc at 2 ft	0	0	0	
Extract, 1:10 in acetone .138 mg/cm^2	15	15	15	

c) Dust: Piperonyl cyclohexenone 5% + pyrethrins 0.004% (referred to as "dust") (Continued)

Insecticide; Method	% Mortality After			
	24 hrs	48 hrs	72 hrs	
Rotenone				
Extract, 2.5% rotenone, 1:400 spray	0	0	0	
Derris (ground), 3.6-4% rotenone, dust	5	45	45	
0.75% dust	0	0	0	
Extract, 1:10 in acetone, 1cc/50cm^2, dried contact	0	10	15	
Extract, 1:800 in 1:1 honey-H_2O, oral	25	30	30	
Derris, ground, 1.5 lb/100 gallons, oral	30	45	45	
Sabadilla				
20% dust, 1g at 2 ft	100	–	–	85% kill in first hour.
" " , " " " (new bees, same cages)	100	–	–	
20% dust, 0.1g at 2 ft	75	80	100	
20% spray, 0.1g/50cm^2 dried 42 hours	100	–	–	100% kill in 3 hours.
above surfaces aged 9 da; (new bees)	–	–	100	
HETP				
6% dust, 1g at 2 ft	100	–	–	80% kill in 3 hours.
" " , " " (same cages; new bees)	100	–	–	
6% dust, 0.1g at 2 ft	50	70	–	
0.1g/50cm^2 dried 18 hr, contact	100	–	–	100% kill in 3 hours.
1:1600 aqueous spray, 4cc at 2 ft	95	100	–	
0.1g/50cm^2 aged 9 da, contact	0	10	20	
Dimethoxy trichloroethane (Dianisyl trichloroethane)				
1:800 in 1:1 honey + H_2O, oral	0	0	0	
1:400, spray	0	0	0	
0.5g/50cm^2, contact spray	100	–	–	
0.1:200 spray	0	0	0	
1:400 in 1:1 honey + H_2O	5	80	85	Ready feeding.
.02g/50cm^2	100			
Phenothiazine				
1g/50cm^2	0	0	0	
1:800 in 1:1 honey + H_2O, oral	0	10	10	

11) Toxicity of pesticide dusts for Apis mellifera, tested under precise conditions of temperature, humidity, time, by the vacuum jar dusting method. Dusts applied at various dosages: 131

Substance (at 400 mg dosages)	Concentration (%)	Mortality (%) At Various Times After Treatment						
		2 hrs	4 hrs	6 hrs	12 hrs	24 hrs	48 hrs	72 hrs
DN 111	10	91	97	100	–	–	–	–
Sabadilla	20	11	51	85	99	100	–	–
Aldrin	2	2	18	35	99	100	–	–
Lindane	1.5	–	60	76	97	100	–	–
Methyl parathion	2	58	67	71	84	100	–	–
Metacide	2	76	76	76	76	100	–	–
Parathion	2	21	39	66	72	100	–	–
Malathion	2	16	23	30	50	100	–	–
EPN	2	60	60	75	90	99	100	–
Endrin	2	0	14	71	96	99	100	–
BHC	2	1	30	50	95	99	100	–
Dieldrin	2	1	19	38	90	99	100	–
Chlordane	5	0	1	18	22	99	100	–
Diazinon	5	0	24	47	71	99	100	–
TEPP	1	36	36	38	90	98	100	–
Heptachlor	2	0	15	49	82	94	100	–
Calcium arsenate	70	2	3	17	54	79	94	100
Perthane (Q-137)	5	0	19	58	83	93	94	95
Isodrin	2	0	0	11	37	72	94	95
DDT	5	1	31	46	73	91	91	91
Compound 1189	5	0	0	1	1	4	54	79
NPD	4	1	24	59	69	71	71	72
Tartar emetic	99	0	7	12	29	41	48	53
Chlorobenzilate	4	0	0	10	34	45	48	50
Cryolite	50	0	0	6	20	28	34	37
Methoxychlor	5	0	6	7	12	36	36	36
Bis-(p-chlorophenyl) ethinyl carbinol (Compound 876)	10	0	1	2	3	3	7	34

Substance	Concentration (%)	Mortality (%) At Various Times After Treatment						
		2 hrs	4 hrs	6 hrs	12 hrs	24 hrs	48 hrs	72 hrs
Ryania	40	0	0	4	21	28	30	31
Toxaphene	10	0	0	1	6	8	26	30
CMU [3-(p-Chlorophenyl)-1,1-dimethyl urea]	10	0	0	1	3	5	26	30
CS 708	5	0	2	6	17	22	26	26
R-242	10	0	2	4	10	23	25	26
1,1-Trichloro-2,2-bis-(p-ethyl phenyl) ethane (Q 128)	5	0	5	5	6	16	21	24
Sulfur	98	0	0	1	2	8	19	24
Aramite®	3	0	0	0	4	15	19	21
DDD	5	3	5	6	9	16	17	20
DNOCHP	10	—	2	4	10	12	13	17
Rotenone	1	0	0	1	6	8	12	16
Ovotran	7.5	0	0	0	7	12	15	15
Chlorinated terpene	5	0	2	3	7	8	12	14
Pyrethrins	0.26	1	2	4	6	8	11	13
Demeton	1	0	0	0	2	5	10	13
Compound 923	10	0	3	4	4	4	9	13
Neotran	7.5	1	2	3	4	6	9	11
CONTROL	—	0	0	1	2	4	7	9
Allethrin	0.26	1	1	1	2	4	6	9
DMC	10	0	0	0	2	3	5	7
Copper-8-hydroxyquinolinate (Cunilate)	5	1	2	3	4	4	5	5
Nicotine	3.6	1	1	1	2	3	3	3
(at 200 mg dosages)								
DN 111	10	91	97	100	—	—	—	—
EPN®	2	31	48	86	99	100	—	—
Sabadilla	20	3	37	80	97	100	—	—
Lindane	1.5	0	0	49	96	100	—	—
BHC	2	0	0	52	93	100	—	—
Heptachlor	2	0	7	46	92	100	—	—
Chlorthion (Compound 22/190)	5	16	55	64	83	100	—	—
Metacide	2	70	72	72	86	100	—	—
Aldrin	2	1	15	32	81	100	—	—
Dieldrin	2	0	0	26	81	100	—	—
Diazinon	5	19	31	54	74	100	—	—
Malathion	2	17	21	26	54	100	—	—
Methyl parathion	2	46	70	90	94	99	100	—
Parathion	2	36	50	66	73	98	100	—
TEPP	1	37	37	37	45	96	100	—
Arsenomethane As-1,2-disulfide	5	1	12	34	55	73	94	96
Isolan	1	3	46	75	87	93	95	95
Endrin	2	0	7	61	86	87	92	92
Chlordane	5	0	1	2	16	46	67	92
Potasan	2	1	4	34	79	81	83	84
O-Ethyl-2-thioethylethyl thionophosphate (Compound 21/116)	2	0	22	36	60	68	73	75
Perthane	5	0	8	46	63	72	72	72
DDT	5	1	11	25	44	61	65	65
Calcium arsenate	70	0	2	3	6	18	45	63
Isodrin	2	1	1	1	11	28	56	62
Compound 1189	5	0	1	1	1	4	36	62
Compound 21/199*	5	0	1	10	22	27	39	44
NPD	4	0	2	14	25	27	28	30
DDD	5	2	3	4	6	15	18	28
Schradan	2	0	1	16	15	21	23	26
Methoxychlor	5	0	1	2	3	23	24	24
DNOCHP	10	0	3	5	18	20	21	23
Toxaphene	10	0	1	3	4	9	18	21
Sulfur	98	0	0	1	1	1	10	17
Rotenone	1	0	0	1	6	8	12	16
1,1-Trichloro-2,2-bis-(p-ethylphenyl) ethane (Q 128)	5	0	0	0	0	11	12	13
Demeton	2	0	1	2	4	5	8	9

* = O,O-Diethyl-O-(3-chloro-4-methyl-4-hydro-7-hydroxycoumarin.

11) Toxicity of pesticide dusts for Apis mellifera, tested under precise conditions of temperature, humidity, time, by the vacuum jar dusting method. Dusts applied at various dosages: (Continued) 131

Substance (at 400 mg dosages)	Concentration (%)	Mortality (%) At Various Times After Treatment						
		2 hrs	4 hrs	6 hrs	12 hrs	24 hrs	48 hrs	72 hrs
CONTROL	—	0	0	1	2	4	7	9
CS-708	5	0	0	0	2	2	3	4
Substance (at 100 mg dosages)								
EPN®	2	8	54	94	100	—	—	—
Lindane	1.5	0	0	38	95	100	—	—
Metacide	2	65	67	69	84	100	—	—
Methyl parathion	2	2	3	48	84	100	—	—
Parathion	2	22	44	57	73	100	—	—
Dieldrin	2	0	0	15	67	100	—	—
BHC	2	0	0	44	98	99	100	—
Diazinon	5	0	6	36	62	98	100	—
Heptachlor	2	0	0	9	71	96	100	—
TEPP	1	28	28	29	47	95	100	—
Aldrin	2	0	12	24	59	99	99	100
Malathion	2	15	20	25	52	99	99	99
Chlordane	5	1	2	3	12	28	50	75
Endrin	2	0	1	31	54	56	61	63
Isodrin	2	1	1	1	7	20	49	54
Compound 1189	5	0	0	0	2	17	34	48
DDT	5	0	1	9	21	44	46	47
Heptachlor	0.5	0	1	2	4	13	36	46
Calcium arsenate	70	0	1	2	5	10	20	28
1,1-Trichloro-2,2-bis-(p-ethylphenyl) ethane (Q 128)	5	3	5	8	16	17	19	23
Perthane	5	0	0	12	16	21	22	22
CMU [3(p-Chlorophenyl)-1,1-dimethyl urea]	10	0	1	1	1	3	11	17
Methoxychlor	5	0	3	4	6	14	15	15
Sulfur	98	0	0	1	2	5	12	13
NPD	4	0	1	6	8	9	9	13
Demeton	1	0	3	3	4	4	9	11
DDD	5	0	0	0	0	4	6	11
CONTROL	—	0	0	1	2	4	7	9
DNOCHP	10	0	3	3	4	6	8	8
Toxaphene	10	0	0	0	2	3	5	7
CS-708	5	0	1	2	4	4	4	4

(1) Highly toxic to bees: DN-111, EPN, Sabadilla, Lindane, BHC, Heptachlor, Chlorothion,® Metacide®, Aldrin, Dieldrin, Diazinon, Malathion, Methyl parathion, Parathion, TEPP®, Compound A-42, Isolan, Endrin, Chlordane.
Moderately toxic to bees: Potasan®, Compound 21/116, Q-137, DDT, Calcium arsenate, Isodrin, Compound 1189, Tartar emetic, Chlorobenzilate, Compound 21/199, Cryolite, Compound 876, Ryania, NPD, DDD, R-242, Schradan, Methoxychlor, DNOCHP, Aramite®, Toxaphene.
Relatively safe for bees: Sulfur, Rotenone, Ovotran®, Chlorinated terpene, Compound Q-128, Pyrethrins, Compound 923, Neotran®, CMU, Demeton, Allethrin, DMC, Cunilate, CS-708, Nicotine.

III) OTHER BENEFICIAL INSECTS

1) Laboratory tests of various insecticides used as dusts on three species of beneficial insects. Adult insects placed on plants previously treated by vacuum dusting: 1404

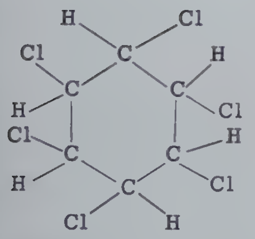
Substance, Concentration As Dust	Insect Mortality (%) In 24 Hours		
	Collops vittatus	Hippodamia convergens	Coleomegilla maculata
DDT, (5%)	38	6	32
Perthane, (5%)	23	6	12
Strobane, (5%)	10	18	12
Heptachlor (2.5%)	41	30	38
Toxaphene (10%)	32	12	36
Endrin (1%)	27	10	18
Dieldrin (2%)	36	4	24

Substance, Concentration As dust	Insect Mortality (%) In 24 Hours		
	Collops vittatus	*Hippodamia convergens*	*Coleomegilla maculata*
Parathion (2%)	65	78	98
Malathion (5%)	47	90	100
Chlorothion (5%)	64	82	100
Diazinon (4%)	37	66	100
CONTROL	11	4	0
Lowest Significant Difference at 5% level.	20	24	26

2) Insecticides and *Orius* sp., *Geocoris* sp., *Chrysopa* sp., *Hippodamia* sp.: 3171
   a) DDT, Toxaphene, Parathion, Dieldrin, Endrin, Demeton: All are toxic to some degree to the above-mentioned beneficial insects.
      (1) Parathion and Toxaphene + DDT mixture are highly toxic.
      (2) Toxaphene, Endrin, DDT are moderately toxic, with DDT the least toxic.
      (3) Demeton has but a limited toxicity.
   b) *Chrysopa* sp. (larvae) and *Orius* sp. are relatively tolerant to a wide variety of insecticides.

13

BENZENE HEXACHLORIDE (BHC; 1, 2, 3, 4, 5, 6-Hexachlorocyclohexane)



Molecular weight 290.85

GENERAL [Refs. 353, 2231, 2815, 3174, 873]

The term benzene hexachloride, BHC, designates a mixture of stereoisomers, known for more than 125 years. A superior general treatment is found in the paper of the discoverers of the insecticidal virtues of BHC, Dupire and Raucourt. As an insecticide, BHC has extraordinary versatility. The active insecticidal ingredient of the isomeric complex is γ-1,2,3,4,5,6-hexachlorocyclohexane (lindane) q.v. A potent stomach poison insecticide which also possesses a persistent contact and fumigant action. More toxic than DDT.

PHYSICAL, CHEMICAL: [Refs. 2579,2848,1751,2638,1853,171]

BHC (crude, tech.): Amorphous, grey-white to brown powder or solid of persistent musty, mousey odor; a stereoisomeric mixture of the $\alpha,\beta,\gamma,\delta,\epsilon$ forms + small amounts of heptachlorocyclohexanes and octachlorocyclohexanes; pure α,β,γ, isomers are known as white, crystalline solids; the physical characteristics of the tech. mixture are variable and not sharply defined. m.p. (tech.): Melting begins at 65°C, the mixture of all isomers melts at 115°-130°C.

Melting point and vapor pressure of individual hexachlorocyclohexane isomers:

	α	β	γ	δ	ϵ	
Amount in Tech.BHC(%)	5	70	12	7	3	
m.p., °C	159-160 158	309-310 312	112-113 112.5	138-139 138	219-220 219	(mixt. decomposes at 288°C)
v.p., mm Hg$^{40°C}$	0.06	0.17	0.14	0.09	-	
v.p., mm Hg$^{20°C}$	0.02	0.005	0.03	0.02	-	
v.p., mm Hg$^{20°C}$	2.5×10^{-5}	2.8×10^{-7}	9.4×10^{-6}	1.7×10^{-5}	-	
v.p., mm Hg$^{60°C}$	0,33	0.58	0.48	0.34	-	

Melting point of impurities: Heptachlorocyclohexane = 85° -86°C; octachlorocyclohexane = 147°-149°C: The α -isomer volatilizes with steam; the β-isomer is nonvolatile with steam, but sublimes.

Solubility: Neither the tech. mixture, nor any of the individual isomers, is soluble in water; the order of solubility in organic solvents is: $\delta > \gamma > \epsilon > \alpha > \beta$. Amount actually soluble in distilled H_2O at 20°C: $\alpha = 10$ppm, $\beta = 5$ppm, $\gamma = 10$ppm, $\delta = 10$ppm.

a) Solubility of hexachlorocyclohexane isomers in various solvents: 2848

Solvent	g/100g Solvent At 20°C			
	α	β	γ	δ
Acetic acid, glacial,	4.2	1.0	12.8	25.6
Acetone	13.9	10.3	43.5	71.1
Benzene	9.9	1.9	28.9	41.1
n-Butanol	1.6	0.7	4.4	19.4
n-Butyl acetate	10.8	7.1	31.5	54.4
iso-Butanol	0.9	0.4	3.0	13.5
Carbon tetrachloride	1.8	0.3	6.7	3.6
Chloroform	6.3	0.3	24.0	13.7
Cyclohexane	1.4	0.8	4.6	2.7
Cyclohexene	5.5	1.0	17.4	14.6
Cyclohexanol	1.9	0.6	4.6	17.3
Cyclohexanone	17.3	12.1	36.7	49.4
Decahydronaphthalene	2.5	0.4	8.7	10.4
Diacetone alcohol	5.4	2.9	21.0	30.5
Diethyl carbonate	10.2	4.1	28.4	46.3
Diesel oil	1.5	0.3	4.1	9.2
Dimethyl acetal	14.3	3.4	38.7	54.7
Dioxane	33.6	7.8	31.4	58.9
Ether	6.2	1.8	20.8	35.4
Ethanol	1.8	1.1	6.4	24.2
Ethyl acetate	12.7	6.9	35.7	58.5
Ethylene dichloride	7.9	0.6	28.9	27.3
Ethylene glycol	0.3	0.1	0.6	4.1
Ethylidene chloride	5.7	0.7	20.2	19.5
Glycerine	0.02	nil	0.06	0.2
Methanol	2.3	1.6	7.4	27.3
Methyl acetate	13.6	6.7	27.7	62.1
Methyl propionate	13.0	7.9	37.8	61.6
Monochlorobenzene	7.4	0.4	23.4	21.4
Naphtha (230°-270°)	5.8	1.5	18.1	30.4
Odorless distillate (198°-257°)	0.8	0.02	2.0	1.1
Paraffin (138°-212°)	1.2	0.05	3.2	4.6
Perchloroethylene	2.4	0.1	7.4	3.5
Pentane	0.9	0.1	2.2	1.6
Petrol ether 40°-60°	0.7	0.1	2.1	1.6
Petrol ether 60°-80°	1.0	0.2	2.7	1.8
Petrol ether 80°-100°	1.0	0.2	2.9	3.2
Petrol ether 100°-120°	1.3	0.2	3.5	3.5
n-Propanol	1.6	1.1	5.2	21.1
iso-Propanol	0.6	0.4	2.8	18.0
Toluene	9.0	2.1	27.6	41.6
Trichloroethylene	3.7	0.3	14.7	7.6
White oil	0.7	0.02	1.9	1.1
Xylene	8.5	3.3	24.7	42.1
H_2O (distilled)	10 ppm	5 ppm	10 ppm	10 ppm

Stable toward light, heat, air, moisture, strong acids. Dehydrochlorinated by alkalis at ordinary temperatures: 1751
$\alpha, \gamma, \delta, \epsilon$ isomers in alkaline alcohol yield 3 moles HCl/mole and 1,2,4-trichlorobenzene (65-86%), 1,2,3-tri- 19
chlorobenzene (5-15%), 1,3,5-trichlorobenzene (6-15%. The β-isomer, dehydrochlorinated by refluxing, yields 644
largely 1,2,4-trichlorobenzene as do the other isomers under the same conditions. Dechlorination rate not 2058
correlated with relative toxicity (for insects) of the isomers. 1299,642

a) The rate constants for alkaline dehydrochlorination at 20°C:

α = ca 0.169 l/sec/mol (K_1); $\beta = 3x10^{-6}$ (K_1); $\delta = 0.110$ (K_2)

γ = 0.045 (K_1) where:

$$C_6H_6Cl_6 + OH^- \xrightarrow{K_1} C_6H_5Cl_5 + H_2O + Cl^-$$
$$C_6H_5Cl_5 + OH^- \xrightarrow{K_2} C_6H_4Cl_4 + H_2O + Cl^-$$
$$C_6H_4Cl_4 + OH^- \xrightarrow{K_3} C_6H_3Cl_3 + H_2O + Cl^-$$

The odor and taste of BHC, which contaminate foodstuffs, are major drawbacks to full use of the insecticidal potential. 1824 2924

a) Reports suggest that chlorination at -8°C, or the refluxing of tech. BHC with aluminum chloride, followed by ether extraction, yield an odorless, tasteless product.

A full treatment of stereochemistry of BHC may be found in Ref. 2231.

Formulations:

1) Wettable powders; dispersible and miscible liquid concentrates; dusts; paints; preparations for vaporization; contact and residual sprays. 2848
   a) γ-Isomer, stable to high temperatures, may be used as an insecticidal smoke.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) LD_{50} values range from 0.3-15g/K for mice, rabbits, rats, cats, sheep, chickens, etc. Acute oral LD_{50} for animals = ca. 1 g/k. 353 185,1290
      (1) Estimated LD of a commercial mixture for man = 0.4g/K. 2221
   b)

Animal	Isomer	Route	Dose	Dosage (mg/k)	Remarks	
Rat	α	or	ca LD_{50}	500		1951
Rat	α	or	LD	1700	(LD_{50} 7 days 1.7 g/k. Ref. 2848)	687
Rat	β	or	ca LD_{50}	> 6000	(No deaths in 7 days Ref. 2848)	1951
Pike*	β	Medium	Toxic	2 ppm	* "And other northern fishes."	603 2026
Mouse	γ	or	LD_{50}	86		805
Rat	γ	or	LD_{50} 7 days	190		2848
Rat	γ	or	LD_{50}	177		805
Rat	γ	or	LD_{50}	200		687
Rat	γ	or	LD_{50}	125		1951
Rat	γ	sc	LD_{50}	50		687
Rat	γ	ip	LD_{50}	35-85	Amount depends on solvent.	596
Guinea Pig	γ	or	LD_{50}	100	In peanut oil.	687
Guinea Pig	γ	or	LD_{50}	127		3362
Guinea Pig	γ	sc	LD_{50}	100	In peanut oil.	687
Rabbit	γ	or	LD_{50}	60		3362
Rabbit	γ	or	LD_{50}	200	In peanut oil.	687
Rabbit	γ	ct	LD_{50}	>4000	Dry inunction.	1952
Rabbit	γ	ct	LD_{50}	>180	In solution.	1952
Rabbit	γ	sc	LD_{50}	75	In peanut oil.	687
Rabbit	γ	iv	LD	4.5-6.0		2208
Goldfish	γ	Medium	Tolerance $Limit_{50}$	0.09 ppm	10 days exposure.	828
Pike*	γ	Medium	Toxic	0.05 ppm	* "And other northern fishes."	603 2026
Fish	γ	Medium	Toxic	1-10 ppm		1192
Rat	δ	or	LD_{50}	900		3063
Rat	δ	or	LD_{50}	1000	(LD_{50} 7 days 1.0 g/k Ref. 2848	1949
Pike*	δ	Medium	Toxic	0.2 ppm	*"And other northern fishes."	
Mouse	BHC(γ12-13%)	or	LD_{50}	700	Commercial preparation of tech. BHC.	1083
Rat	BHC(γ12-13%)	or	LD_{50}	1250	Commercial preparation of tech. BHC.	2849 3064
Goldfish	BHC(tech)	Medium	Tolerance $Limit_{50}$	0.24 ppm	10 days exposure.	828
Trout	BHC(tech)	Medium	Disabling	1 ppm	As an emulsion.	595
Trout	BHC(tech)	Medium	Disabling	10 ppm	As acetone solution.	595
Goldfish	BHC+DDT	Medium	LC_{50}	3 ppm	10 days exposure.	827

   c) General remarks on toxicity of BHC:
      (1) Toxicity of tech. and commercial samples varied with isomer proportion (particularly the amount of γ-isomer present) formulation and animal tested. 2848 1949,2849
         (a) Average toxic dose for mammals in general = 125 mg/k γ-isomer.
         (b) Toxic dose (man) is less than that of DDT, but BHC is not readily absorbed by skin, mouth. 1221,448
      (2) LD_{50} values of 2 early preparations for mice, rats, rabbits, guinea pigs, cats, sheep, chickens, pigeons = 1000-15,000 mg/k. 1290
      (3) For some fish less toxic than DDT; bluegills tolerated 0.45 ppm. 215
         (a) Trichlorobenzene, dehydrochlorination product of BHC, is toxic in low concentration to fish. 3019
      (4) Highly toxic to some invertebrates (e.g. isopods) other than insects. 2302,1507
         (a) No apparent toxic effect on earthworms.
   d) Sub-acute effects; chronic toxicity; tolerated and sub-lethal dosages: 3277
      (1) Comparative toxicity BHC, DDT, methoxy-DDT, chlordane, for livestock:

Insecticide	Animal	Wgt (lbs)	Dosage (g/k)	Results
BHC(10%γ)	Sheep	86	2	Extreme symptoms in 6 hrs: Spasms, blindness; normal 5th day.
BHC(10%γ)	Sheep	124	1	Slight nervous symptoms in 24 hrs. Quick recovery.

(1) Comparative toxicity BHC, DDT, methoxy-DDT, chlordane, for livestock: 3277

Insecticide	Animal	Wgt (lbs)	Dosage (g/k)	Results
BHC(10%γ)	Sheep	90	0.75	Slight nervous symptoms in 24 hrs. Normal in 48 hrs.
BHC(10%γ)	Steer	710	0.125	No effect.
DDT	Sheep	85	2	Extreme nervousness, spasms in 24 hrs—5 days, Normal 9th day.
DDT	Sheep	97	1	Muscle tremors, incoordination; normal in 48 hrs.
DDT	Sheep	93	0.5	Slight nervous symptoms for 24 hrs.
DDT	Steer	540	0.5	Nervous twitching, incoordination; normal on 6th day.
methoxy-DDT	Sheep	115	1	No effect.
methoxy-DDT	Sheep	83	2	No effect.
methoxy-DDT	Steer	540	0.5	No effect.
chlordane	Sheep	78	2	Severe nervous and respiratory symptoms 16 hrs; death in 48 hrs. 3277
chlordane	Sheep	123	1	Severe nervous and respiratory symptoms 16 hrs; death in 48 hrs.
chlordane	Sheep	103	0.5	Incoordination, nervousness, blindness; normal in 5-6th days.
chlordane	Steer	820	0.05	No effect.

(2) Cattle reported unaffected by 75,125 mg/k. Calves: Severe harm at 300 mg/k. 3277,1083,3330

(3) Dogs tolerated with little effect 400 mg/k BHC containing 35% γ-isomer. 1083

(4) Rats: Highest levels tolerated without tissue damage when given in diet for 104 weeks: 2231

(a) Tech. BHC - 10 ppm
(b) α-Isomer - 10 ppm
(c) β-Isomer - $<$ 10 ppm
(d) γ-Isomer - 50 ppm
(e) δ-Isomer - $<$ 800 ppm

(5) Rats: Dietary levels at which gross effects ensued: 2231

(a) Tech. BHC - 100 ppm
(b) α-Isomer - 100 ppm
(c) β-Isomer - 10 ppm
(d) γ-Isomer - 100 ppm

(6) Rats: γ-Isomer, non-toxic at 200 ppm in diet for 4 wks; growth reduction at 400 ppm; fatal to many at 600 ppm; fatal to 75% at 800 ppm. 817

(7) Rats: Tolerated, with normal growth, 500 mg/k in diet for 57 days. 3064

(8) Rats: Tolerated γ-isomer at 30 mg/k/day. 3064

(9) Rats: Retarded growth when fed β at 100ppm, α at 800ppm, γ at 1000ppm, BHC tech. at 800ppm. 1016

(10) Mice: Survived 40mg/k, distributed in oral doses over a period of 30 days. 1083

(11) Cattle: Tolerated 125 mg/k/week, orally, to protect from tsetse fly, ticks. 3330

(12) Comparative effects, chlorinated hydrocarbon feeding. Dogs: 203

Substance	Dosage (mg/k) (active ingredients)	Total Given (mg)	Estimated Total (active ingredients)	Sex	Results
BHC (wettable)	5	1,188.69	71.35	♀	No effect.
" "	10	2,684.94	159	♂	No effect.
" "	15	1,699.32	102	♂	No effect.
" "	20	4,389.58	264	♂	No effect.
BHC tech. (33-36% γ)	100	6,504	2168	♂	No effect.
" " " "	200	12,816	4272	♂	No effect.
" " " "	300	12,681	4227	♂	Slight diarrhoea, nervousness, dilated pupils.
" " " "	400	11,160	3720	♂	No effect.
6% γ-isomer	25	5,110.46	306.8	♀	No effect.
" " "	50	13,244.7	795	♂	No effect.
" " "	60	13,164.7	790.8	♂	Slight diarrhoea, vomiting, anorexia.
" " "	75	8,496.6	510	♂	Slight diarrhoea, vomiting, anorexia.
Toxaphene (25% chlorinated camphene)	20	636	159	♂	Convulsions, extreme salivation in 12 hrs.
" "	30	1,008	252	♂	Convulsions, tremor, diarrhoea in 2 hrs.
" "	40	1,017.6	254.4	♀	Convulsions, tremors in 12 hrs.
" "	50	1,544	386	♀	Convulsions, kill in 3 hrs.
" "	60	2,289.6	572.4	♂	Convulsions, kill in 2 hrs.
" "	70	2,226	556.5	♂	Convulsions, kill in 3 hrs.
" "	80	2,035.2	508.5	♀	Convulsions, kill in 3 hrs.
Chlordane (wettable 50% active ingredient)	200	7,224	3862	♂	Clonic spasms in 12 hrs.
" "	225	5,931	2065.2	♀	No effect.
" "	250	5,110	2555	♀	Slowed respiration.
" "	300	11,586	5793	♂	Clonic spasms, tremor in 4 hrs.
Chlordane (wettable)	400	10,544	5272	♀	Tremors, salivation, convulsions, blindness.
" "	500	10,220	5110	♀	Tremors, convulsions, prostration.
" "	700	6,356	3178	♂	No effect.

(13) Mammals in general: Toxic level = 400 ppm daily intake in the diet. 1949

(14) Effects of topical application: Dips, sprays, dusts, inunctions:

  (a) Man: Used as scabicide without adverse effect. Application of 15-20g of 1% mixture in vanishing cream or lotion over entire skin surface of adult and allowed to remain 24 hrs. was effective in scabies without apparent dermal absorption hazard. Second, third applications at weekly intervals were without hazard. Sensitization, irritation at this dosage not reported. Available as 1% BHC (U.S.P.) lotion, ointment under various proprietary names. 1221

  (b) Animals: γ-Isomer hazardous in 1 inunction at 50 mg/k; repeated inunction at 20 mg/k; irritating. 1949

  (c) Cattle: Single spray, 1.5% suspension γ-isomer gave 100% kill; 0.05% emulsions γ-isomer were fatal for calves; 0.25% spray harmless for adult cattle. Maximum Tolerated Dose; Calves = < 0.05% suspension as single spray. Sheep, goats, pigs tolerated single dips, sprays with 0.5% γ-isomer. 407 2571

  (d) Cattle survived 1 dip in 5% γ-isomer suspension without symptoms. 407

  (e) Cattle, sheep, goats, pigs, horses survived without symptoms 8 dips within 1 month in 1.5% γ-isomer suspensions. 407

  (f) Rats tolerated, without symptoms, daily cutaneous application for 14 days of 5% emulsions, γ-isomer, to ears and tail. 2850

  (g) Mice, prevented from grooming, survived 1 dip in 5% γ-isomer emulsion; died following 1 dip in 10% emulsion. 2850

  (h) Dogs, cats: Safe as 0.5% γ-isomer dry dusts; frequent use on cats hazardous. 2571

  (i) Poultry: unsafe, hazardous, and not to be applied directly. 2571

(15) General remarks:

  (a) Danger as a chronic toxicant: When properly used, minimal and less than that of DDT. Range cattle withstood, without clinical signs, 10 applications at 2 week intervals of 0.2% wettable powders. 2571

  (b) On young animals: Use against lice, fleas, ticks, mites, biting flys is limited by toxic hazard; not to be applied to calves under 3 months of age; for poultry, use only as a roost paint. 129

  (c) Special care is recommended in mixing concentrates. Contaminated skin is to be washed at once, contaminated clothing removed at once. Avoid breathing of vapors, dusts, sprays, and the contamination of food for men and animals. 2345

  (d) The mammalian toxicities of the isomers differ: 2120
  α:-Low acute, chronic, cumulative toxicity.
  β:-Low acute; high chronic, cumulative toxicity.
  γ:-Some acute mammalian toxicity; not a chronic, cumulative poison.
  δ:-Low acute, chronic toxicity; irritant to mucous membranes.

  (e) Residues present a problem because of odor and taste, and the cumulative, chronic toxicity potential of some isomers. 129

  (f) Only the γ-isomer is effective for livestock pests; most animals tolerate it well. 2571

PHARMACOLOGY; BIOCHEMICAL, PHYSIOLOGICAL ACTION; SYMPTOMATOLOGY:

1) The acute symptoms of intoxication are those of central nervous stimulation with rise in blood pressure, fall in heart rate; encephalogram of the Grand Mal type. These symptoms are ascribable to the γ-isomer. The β, δ isomers are central nervous system depressants. 2208

  a) In laboratory animals: Excitation, hypersensitivity, tremor, spasms, convulsions, ataxia, paralysis and death. 1290 2208

    (1) Tremor, convulsion controlled by barbiturates (e.g. pentobarbital) and partly by β and δ -isomers, which are CNS depressants. 2208

  b) In older cattle: Hypersensitivity, tremors and finally general paralysis. 3330

  c) In calves: Hyperstimulation, profuse salivation, eye-rolling, grinding of teeth, twitching, excited behavior, convulsions and/or depression, dullness, anorexia, refusal to drink, blindness and finally opisthotonus, limb threshing and agonized death. 407

2) BHC counters the convulsive symptoms of metrazole, picrotoxin, nikethamide. 1499

3) In man: The onset of symptoms may come in 1-2 hours, death in 24 hours. 129

  a) Oil and epinephrine to be avoided in treatment of BHC poisoning. 129

4) Histological and histopathological changes have been noted in liver, kidney, bladder, gastrointestinal tract, heart, lungs, brain, and nerve cord. 407 1083,3330

  a) Fat droplets accumulate in cells of many organs. 185

5) Enlargement of liver, with hepatic cell swelling, in chronic intoxication. 1016,1953

6) With regular intake of BHC, storage occurs in the tissues, particularly in fat. Maximum accumulation occurs in 6 weeks. Appears in milk of lactating animals. 1016 2571

  a) Elimination is rapid when intake stops; β-isomer more persistent than others. 2571,708

  b) γ-Isomer appears in rat tissues (fat) shortly after feeding of 20 and 1000 ppm begins, but there is no accumulation. 1928

  c) γ-Isomer is rapidly metabolized in vivo. 1950

7) Experimental evidence does not support the theory that BHC serves as an antimetabolite for inositol in cell metabolism. 817, 2848,1004,2208

PHYTOTOXICITY:

1) At insecticidal levels not generally hazardous, except to cucurbitaceae, but at higher levels BHC interferes 129
with seed germination, growth, yield and may cause root deformation and cytogenetic changes by induction of 1853
polyploidy (a colchicine-like effect). 2898
   a) generally more toxic than DDT for plants; highly toxic to most germinating seeds and to roots. 294
      (1) Corn is sensitive; muskmelons extremely sensitive; snap-beans are tolerant and strawberries unusually tolerant. 294
      (2) Markedly injurious to seed germination at 1-6 lbs/acre. Bean and corn seeds were seriously injured by coating with BHC dusts. 294
      (3) 3 ppm (6 lbs/acre, soil $6\frac{2}{3}$ in deep) injurious to red clover, vetch, soybean; 30 ppm do serious injury. Harmful at 20-50 lbs/acre to wheat, oats, barley. Reported harmless to grain grops at 15 lbs/acre. 294
      (4) At 50-80 lbs/acre, not harmful to cotton, tobacco, the following year; 100-200 lbs/acre have consistently ruined experimental plantings. 294
      (5) Some potato varieties tolerated 80 lbs/acre; others were injured by 20 lbs/acre. 294
   b) Must not be used with potatoes, sweet potatoes, carrots, beets, or other root crops, or with peanuts or any plant whose edible parts develop in the soil. BHC taints the flavor of such crops with a bad taste and unpleasant odor. 294
      (1) May, in addition, taint the meat, milk, butter of animals pastured on treated forage or given treated 129
      food. 2120
   c) Pound for pound, lindane (γ-isomer) is as toxic as tech. BHC. However, since only $\frac{1}{8}$ as much is required for an equivalent effect in insect control, much smaller quantities reach the soil. 294
   d) Soil microflora: At 100-500 lbs/acre, soil fungi and nitrifying bacteria are suppressed for several months. 294
   e) Persistence, soil accumulation:
      (1) Less persistent than DDT. Large doses decompose at rate of 10% per year. 294
      (2) Toxic effects for sensitive crops persist for 5 years on soils originally receiving 100-200 lbs/per acre. 294
      (3) The accumulation tendency is less than that of DDT, but accumulation occurs on soils receiving substantial dosages. 294

2) Degree of plant injury due to BHC used at a rate giving a dosage of 27.5 lbs γ-isomer/acre (1.01 lbs/1000 ft^3). 2304

Plants Totally Destroyed	Plants Partly Susceptible To Injury	Plants Not Injured
Beet, (Detroit Dark Red)	Beans (bush), (Burpee Stringless)	Broccoli, (Italian)
Cantaloupe, (Hale's Best)	Beans (pole), (Rogers, Blue Lake, Associated 12)	Cabbage, (Golden Acre)
Chard, (Giant Lucullus)	Beans (Lima), (Burpee's Bush)	Carrots, (Chantenay)
Corn, (Hummer, Golden Cross Bantam)	Endive, (Green, Curled)	Celery (sets), (Utah Green)
Cucumber, (Boston Pickling)	Lettuce (from seed), (Grand Rapids)	Kohlrabi, (Early Purple)
Onion, (White Bermuda)	Lettuce (sets), (New York Head)	Mustard, (Southern Curled)
Peas, (Blue Bantam)	Pepper (sets), (California Wonder)	Parsnips, (Hollow Crown)
Potatoes (White Rose)	Tomato (sets), (Chatham, Golden Jubilee, Pritchard, Bonny Best, Stokedale)	Radish, (Crimson Giant)
Pumpkin (Pie)		Rutabaga
Spinach (Noble Giant)		
Squash (Table Queen, Crookneck)		
Tampala		
Tomato (from seed) (Bonny Best)		
Watermellon (Klondike)		

   a) Control, lasting over 5 months, of the following weeds: Chenopodium album, (lamb's quarter), Amaranthus retroflexus, (pigweed), Convolvulus arvensis, (bindweed) was had with BHC. 2304
   b) No effect noted on weed grasses or Senecio vulgaris, (groundsel). 2304

3) Additional observations on phytotoxicity:
   a) May scorch or injure radish, turnip, kale, spinach, and beet seedlings. 2988
   b) Used as a greenhouse "smoke," may damage roses. 482
   c) Used at 30 lbs/acre, damages squash foliage. 482
   d) As 3% dust damaged cantaloupe, cucumber at 30 lbs/acre; as 1% dust at 175 lbs/acre injured sweet corn. 349
   e) As 0.1% suspensions, injurious to tobacco seedlings. Above 1.6 lbs (tech.)/acre BHC suppressed root 820
   development in seedling tobacco. BHC (tech.) dust at 2.25 lbs/acre on 11 day seeding tobacco gave tem- 123
   porary stunting and distortion; to 11 lbs/acre the effect was transitory. At 37.5 lbs tech. BHC/acre many plants were killed, others seriously stunted. Considerable mortality in 3 week old tobacco at 75.6 lbs tech. BHC/acre.
   f) At 275 lbs/acre injurious to lettuce, pepper, beans, tomatoes, beets, cantaloupe, chard, corn, cucumber, onion, peas, potatoes, pumpkin, spinach, squash, watermelon. 1262
   g) Injurious to roots of peas at 60 lbs/acre. 2726
   h) Growth of legumes inhibited by 30 ppm in soil. 3325
   i) 200 ppm in soil injured onions; 800 ppm killed onions. 2204
   j) 200 ppm in soil injurious to wheat, flax, cabbage, beet, cress; 25 ppm was injurious to oats. Rye is the least susceptible cereal. 2898
      (1) γ-Isomer apparently not the phytotoxic principle. 80
      (2) δ-Isomer alone found toxic for leaves, stems. 2698
   k) Applied in sand culture to Norway pine seedlings at a rate equivalent to 1 ppm crude BHC and 8 oz γ-isomer/acre, root malformations resulted. 2838

(1) Polyploidy, multinucleate cells, cytological malformations of the root tip meristem, increased in chromosome number (aneuploidy) resulted.

(2) A colchicine-like response after 8.5 days exposure gave disruption of the achromatic figure, extrustion of chromosomes from nucleus, chromatids attached at centromere only.

TOXICITY FOR INSECTS

1)

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti (adult)♂	Topical (spray)	LD$_{50}$	3 μg/g	Given by author as 3 mg/k γ-isomer.	693
Aëdes aegypti (adult)♀	Topical (spray)	LD$_{50}$	3.5 μg/g	Given by author as 3.5 mg/k γ-isomer.	693
Anopheles quadrimaculatus (larva)	Medium	LC$_{100}$*	0.2 ppm	*Least ppm for 100% kill, 0.1 ppm gave 92% kill.	2020
Anopheles quadrimaculatus (larva)	Medium	LC$_{100}$ 24 hr	1 ppm	Crude BHC; 0.1 ppm gave 81.6% kill.	762
Apis mellifera (adult)	or	LD$_{50}$	0.15 μg/bee	BHC, 90% γ-isomer.	910
Blattella germanica	Topical	LD$_{50}$	3.8 μg/g	γ-Isomer.	1757
Blattella germanica	Contact (residue)	MED**	0.1-0.5 mg/1000cm^2	**=Minimum Effective Deposit. As BHC.	1367
Blattella germanica	Contact (residue)	MEMP***	10 min on 0.5 mg/1000cm^2	***= Minimum Exposure for Maximum Paralysis.	1367
Cimex lectularius	Topical (spray)	LC$_{50}$	0.051%	γ-Isomer in P31 oil sprayed at 0.36 mg/cm^2	413
Cimex lectularius	Topical (spray)	LD$_{50}$	0.023 μg/insect (6 mg/k)	γ-Isomer.	413
Epilachna varivestis (adult)	Topical	LD$_{50}$	0.0574 (.0493-.0668) mg/g	γ-Isomer in acetone.	2822
Epilachna varivestis (4th instar)	Topical	LD$_{50}$ 6 days	0.0473 (.0382-.0568) mg/g	γ-Isomer in acetone.	2822
Epilachna varivestis (adult)	Topical	LD$_{50}$ 6 days	3.12 (0.739-11.1) mg/g	δ-Isomer in acetone.	2822
Epilachna varivestis (4th instar)	Topical	LD$_{50}$ 6 days	1.83 (0.344-4.79) mg/g	δ-Isomer in acetone.	2822
Leptinotarsa decemlineata	Topical (dust)	LC$_{50}$ 2 days	4%	BHC in talc.	873
Leptinotarsa decemlineata	Topical (dust)	LC$_{85}$ 4 days	4%	BHC in talc.	873
Melanoplus differentialis	Topical (spray)	LD$_{50}$	3.4 μg/g	γ-Isomer.	1757
Melanoplus differentialis	or	LD$_{50}$	[illegible].7 μg/g	γ-Isomer in baits.	1757
Melanoplus differentialis	or	LD$_{50}$ 24 hr	5-10 μg/g	In xylene emulsion. γ-isomer.	1756
Melanoplus femur-rubrum	Topical	LD$_{50}$	0.013-0.11 mg/g	BHC (37% γ-isomer).	3266
M. femur-rubrum	or	LD$_{50}$	ca 0.035 mg/g	BHC (37% γ-isomer).	3266
M. femur-rubrum	or	LD$_{50}$	0.005-0.01 mg/g	γ-Isomer.	1756
Musca domestica (adult)♂	Topical (spray)	LD$_{50}$	2.0 μg/g	Given by author as 2.0 mg/k. In kerosene.	693
Musca domestica (adult)♀	Topical (spray)	LD$_{50}$	3.0 μg/g	Given by author as 3.0 mg/k. In kerosene.	693
Musca domestica (adult)	Topical (spray)	LC$_{90}$	0.17%	γ-Isomer.	1094
Oncopeltus fasciatus	Topical	LD$_{50}$	32.5 μg/g	γ-Isomer.	1757
Oncopeltus fasciatus (adult)♂	Topical	LD$_{50}$ 6 days	2.48 (1.87-3.27) μg/g	78°F. γ-Isomer in acetone on ventrum.	2822
Oncopeltus fasciatus (adult)♀	Topical	LD$_{50}$ 6 days	2.89 (2.56-3.27) μg/g	78°F. γ-Isomer in acetone on ventrum.	2822
Pediculus humanus corporis	Topical (spray)	LC$_{50}$	0.016%	γ-Isomer in P31 oil, sprayed at 0.36 mg/cm^2.	413
Pediculus humanus corporis	Topical (spray)	LD$_{50}$	0.003 μg/insect	1.5 mg/k.	413
Periplaneta americana	Topical	LD$_{50}$	5 μg/g	γ-Isomer in acetone.	2744
Periplaneta americana	inj	LD$_{50}$	4 μg/g	γ-Isomer, intra-abdominal.	2744
Periplaneta americana	inj	LD$_{50}$	17 μg/g	γ-Isomer as emulsion intra-abdominal.	846
Prodenia eridania (5th instar)	or	LD$_{50}$ 4 days	21.9 (20.1-23.8) μg/g	γ-Isomer in leaf sandwich; (av. wgt. insect 0.4g av. length insect 3-3.5cm).	2822
Prodenia eridania (5th instar)	or	LD$_{50}$ 4 days	1050 (855-1300) μg/g	δ-Isomer " " " "	2822
Sitophilus granarius	Medium	LC$_{50}$ 5 days	0.4 ppm	γ-Isomer as dust by weight in grain.	2848
Tribolium castaneum	Medium	LC$_{50}$	0.142 mg/g medium	Medium = wheat flour; γ-isomer.	2823
Tribolium castaneum	Medium	LC$_{50}$	27.6 mg/g medium	Benzene heptachloride mg/g wheat flour	2823
Calliphora spp (adults)	Topical	LD$_{50}$ 48 hr	0.6 μg/g	γ-Isomer in acetone.	2744

2) Relative toxicity of hexachlorocyclohexane isomers for various insects: 2232

Test Insect	Route	BHC Isomer					
		γ	α	β	δ	ϵ	
Oncopeltus fasciatus	Topical	1	>3700	>1800	>7400	>2500	2822
Epilachna varivestis	Topical	1	> 520	> 220	55	> 410	2822
Prodenia eridania	or	1	> 97	> 53	48	> 110	2822
Heliothrips haemorrhoidalis	Residue	1	1000	>10,000	10,000	>10,000	2227
Oryzaephilus surinamensis	Residue	1	70	–	88	–	2040
Macrosiphoniella sanborni	Residue	1	non-toxic	–	16	–	2040
Sitophilus (=Calandra) granarius	Residue	1	900	>5000	5500	–	2848
Anopheles quadrimaculatus	Medium	1	250	>10,000	> 250	–	642
Musca domestica	Residue	1	>10,000	–	1300	>10,000	157
Blattella germanica	Dipping	1	28	–	300	147	157
Tribolium confusum	Residue	1	2800	–	7.3	53	157
Aëdes aegypti	Medium	1	>1600	–	>1600	1500	157

3) Resume´ of insects and other pests effectively controlled by BHC in practical economic dosages: 2848

a) Orthoptera: Locusta migratoria, Gryllus domesticus, Blattella germanica, Blatta orientalis.
b) Anopleura: Pediculus humanus.
c) Hemiptera: Cimex lectularius
d) Lepidoptera: Various leaf-eating larvae for example Pieris spp., Cheimatobia brumata, Tineola bisselliella, Diaphania hyaliniata, Laphygma eridania, Pachyzancla bipunctalis.
e) Coleoptera: Various flea beetles, Phyllotreta spp., Phaedon cochlearis, Meligethes aeneus, Anthonomus pomorum, Sitones lineata, Calandra granaria, Dermestes vulpinus.
f) Hymenoptera: Various wasps, Vespidae, Ants, for example Lasius spp.
g) Diptera: Various mosquitoes for example Aëdes aegypti, Anopheles gambiae, Anopheles maculipennis, Theobaldia spp., etc., Musca domestica.
h) Siphonaptera: Various fleas for example Ctenocephalis spp.
i) Arachnida: Dermanyssus gallinae.
j) Crustacea: Woodlice, Oniscidae spp.

2822

4) Quantitative data: Relative toxicity of BHC isomers for various insects:

a) By topical application in acetone solution to the ventrum; mortality at 6 days after treatment corrected; insects held at 78°F.

(1) Oncopeltus fasciatus adult, 10-60 individuals/trial.

Isomer	Amount (mg/g)	♂ % Mortality (corrected)	Amount (mg/g)	♀ % Mortality (corrected)
α	9.23	32	9.94	19
	4.42	0	4.31	14
β	4.52	0	4.64	7
γ	.0175	100	.0175	100
	.0165	100	.00837	93
	.00871	95	.00596	95
	.00679	95	.00452	65
	.00522	79	.00350	62
			LD$_{50}$ .00289 (.00256-.00327)	
	.00438	53	.00255	39
	.00342	66	.00173	27
		LD$_{50}$ .00248 (.00187-.00327)		
	.00246	51	.00809	3
	.00167	44	.000329	0
	.000781	6		
	.000315	2		
δ	18.5	22	19.9	25
	9.23	11	9.94	14
	4.42	6	4.31	0
ϵ	6.33	0	6.4	0
acetone (112 insects)		5	(100 insects)	7
acetone (14 insects)		7	(33 insects)	12

(2) Epilachna varivestis ♂ ♀

		adults (10-80/trial)		4th Instar (10-50/trial)
α	29.7	0	44.8	9
	12.8	0	17.6	0
β	12.6	0	17.6	0
γ	0.62	100	.915	100
			.604	100
	0.572	100	.366	100
			.277	92
	.243	100	.185	87
	.122	85	.0963	82
	.0848	69	.0723	35
		LD$_{50}$ .0574 (.0493-.0668)		LD$_{50}$ .0473 (.0382-.0586)
	.0573	56	.0380	45
	.0186	3	.0196	28
			.00723	3
			.000624	0
δ	12.6	70	89.5	100
			44.8	100
	5.96	90	19.2	78
	2.38	59	13.1	64
	LD$_{50}$ 3.12 (.739-11.1)			
	1.28	25	9.55	70
	0.657	4	3.69	68
	0.297	7	1.94	68
				LD$_{50}$ 1.83 (.344-4.79)
			.989	46
	0.0572	0	.396	11
ϵ	23.4	8	24.1	22
			20.0	15
Benzene heptachloride	23.3	95	11.9	100
			6.13	100
	17.5	96	5.67	90
			4.51	85
	11.9	92	3.07	69
			2.54	59
	5.71	69	1.32	27

Isomer	Amount (mg/g)	% Mortality (corrected) adults	Amount (mg/g)	% Mortality (corrected) 4th instar
	2.97	41	.75	13
	1.43	25	.67	8
	0.69	12	.58	8
	.33	0	.36	2
acetone (50 insects)		2	(99 insects)	7
acetone (61 ")		3	(44 ")	2

(3) Prodenia eridania: 5th instar, ca. 0.4g weight, 3-3.5cm length; oral route, leaf sandwich feeding; mortality 4 days after treatment; insects held at 78°F; 8-65 insects/trial:

Isomer	Dosage (mg/g)	% Mortality (corrected)
α	2.14	0
β	1.26	0
γ	.0624	100
	.0540	100 (LD$_{50}$ .0219
	.0448	100 (.0201-.0238))
	.0360	89
	.0245	55
	.0148	20
δ	2.79	100
	2.28	82 (LD$_{50}$ 1.05
	1.72	76 (.855-1.30))
	1.28	75
	.63	13
	.40	0
ϵ	2.47	0

(4) Tribolium castaneum: BHC isomer toxicity; applied in wheat flour medium: 2822 2823

Isomer	mg/g Flour	No. Insects	% Mortality
α	100	200	0.5
β	50	200	1.0
γ	0.5	300	99.0
	.4	300	99.3
	.3	300	97.0
	.2	300	78.3
	.15	300	58.7
	.125	300 (LC$_{50}$ .142 mg/g flour)	34.3
	.1	300	25.3
	.09	300	12.3
δ	100	200	3.5
ϵ	100	200	1.0
Benzene hepta-chloride	30	300	46.7
	25	300 (LC$_{50}$ 27.6 mg/g flour)	48.0
	20	300	34.0
	15	300	23.7
	10	300	2.0
acetone		750	0

5) Comparative toxicity of BHC isomers used as fumigants. No contact with isomers except as vapours. 2822

a) Fumigation carried on in 970 cc jars, the atmosphere maintained at saturation with the respective isomers by use of 5-10g amounts; mortality 4 days after exposure:

b) Insects: I = Tribolium castaneum adult 100-300/trial; II = Hyphantria textor, larvae 6th instar 10-20/trial; III = Epilachna varivestis adult.

Isomer	Temperature (°F)	Exposure (hrs)	% Mortality (corrected) I	II	III
α	59	24	0	0	0
"	68	24	0	0	0
"	86	24	1	0	0
β	59	24	0	0	0
"	68	24	0	0	0
"	86	24	0	0	10
γ	59	4	0	30	10
"	59	8	1.3	35	3
"	59	24	80.7	55	10
"	68	4	22.7	35	3
"	68	8	56.7	50	3
"	68	24	92.7	70	44
"	86	4	58.7	10	5
"	86	8	75.3	60	32
"	86	24	99.7	100	96
δ	59	24	0	0	0
"	68	24	1	20	0
"	86	24	1	0	6
ϵ	59	24	—	—	0
"	68	24	—	—	0
"	86	24	—	—	5
Benzene heptachloride	59	24	—	—	0

b) Insects: I = Tribolium castaneum adult 100-300/trial; II = Hyphantria textor, larvae 6th instar 10-20/trial; III = Epilachna varivestis adult.

Isomer	Temperature (°F)	Exposure (hrs)	% Mortality (corrected)		
			I	II	III
Benzene heptachloride	68	24	—	—	0
" "	86	24	—	—	0
Control	59	—	0	0	0
"	68	—	0	0	0
"	86	—	0	0	0

c) Oncopeltus fasciatus, adult, 30-50/trial; fumigation carried out as specified above in "a."

Isomer	Temperature (°F)	Exposure (hr)	% Mortality (corrected)
α	59	24	13
"	68	24	33
"	86	24	72
β	59	24	10
"	68	24	0
"	86	24	14
γ	59	1	30
"	59	2	23
"	59	3	70
γ	59	4	90
"	59	8	100
"	59	24	100
"	68	1	47
"	68	2	93
"	68	3	100
"	68	4	100
"	68	8	100
"	68	24	100
"	86	1	80
"	86	2	100
"	86	3	100
"	86	4	100
"	86	8	100
"	86	24	100
δ	59	24	0
"	68	24	0
"	86	24	10
ε	59	24	0
"	68	24	0
"	86	24	0
Benzene heptachloride	59	24	0
" "	68	24	0
" "	86	24	30
Control	59	—	0
"	68	—	5
"	86	—	5

d) Time of exposure to air saturated with BHC, γ-isomer, needed to give 50% mortality 4 days after treatment: 2822

Insect	Temperature (°F)	Time of Exposure (hrs)
Oncopeltus fasciatus	59	2.1
" "	68	1
" "	86	<1
Tribolium castaneum	59	17.5
" "	68	7.1
" "	86	3.4
Epilachna varivestis	59	>24
" "	68	26.4
" "	86	9.8
Hyphantria textor	59	17.2
" "	68	8.3
" "	86	7.2

6) Relative toxicity of BHC-isomers and related substances:

a) As dusts: Amount required as dusts applied to grain to give 50% kill in 5 days of Sitophilus granarius [Ref. 2848]

b) As spray: % concentration required for LC_{50} (50% kill) of Heliothrips haemorrhoidalis [Ref. 2227]

Isomer	Rel. amt. by wgt for 50% kill	Amount for 50% kill	LC_{50} (%)
α	900	360 ppm	0.1
β	practically non-toxic	practically non-toxic	>1.0
γ	1	0.4 ppm	0.0001
δ	5500	2200 ppm	1.0
DDT	15		

(1) Of the following substances spray concentrations greater than 0.1% were required to give 50% kills of H. haemorrhoidalis: 2227
ε-BHC; α-heptachlorocyclohexane; β-heptachlorocyclohexane; β-1,1,2,3,4,4,5,6-octachlorocyclohexane; α-1,1,2,2,3,4,5,6-octachlorocyclohexane; β-1,1,2,2,3,4,5,6-octachlorocyclohexane; 1,1,2,2,3,4,4,5,6-enneachlorocyclohexane; 1,2,3,4,5,6-hexabromocyclohexane; 1,2,4-trichlorobenzene.

(2) Toxicity of γ-isomer for H. haemorrhoidalis was not influenced by presence of other isomers, alone or in combination.

b) Comparative toxicity of BHC isomers as solutions, w/w, in odorless distillate spray, for Musca domestica: 2848

Isomer	Concentration Of Spray w/w	Mortality %
α	0.8 (saturation)	21
γ	0.01	73
δ	1.1 (saturation)	24
DDT	0.02	51

7) BHC, and isomers of BHC, as fumigants, smokes:

a) The fumigating action of BHC recommends it as an insecticide for insects inhabiting crevices of vegetation, crinkled leaves (spinach etc.) 2848

b) As a smoke in the open air at a dosage of 102 lbs γ-isomer/acre, control of Glossina palpalis to the degree of 80-90% has been obtained. 1550

(1) Time, in hrs, for 100% kill of various insects exposed in space of 253 in^3 at 75°F, 62% relative humidity: 2946

Insect	Stage	Time (hrs) For 100% Kill BHC/253 in^3 2.5g	5g
Blattella germanica	adult	70	60
Dermestes lardarius	adult	216	216
D. lardarius	larva	240	232
Ephestia küehniella	adult	16	16
E. kuehniella	larva	168	168
Malacosoma americana	larva	96	80
Oryzaephilus surinamensis	adult	144	144
Tribolium confusum	adult	260	250
Trogoderma sternalis	adult	65	53
T. sternalis	larva	228	212

(2) Initial kills by insecticidal smokes: γ-BHC, DDT: 426

Insect	Conditions	% Mortality (24 hr after exposure) DDT	γ-BHC
Culex molestus adult	Under 1 layer straw matting	100	100
Culex molestus adult	" 2 layers " "	100	100
		% kill (7 days after exposure)	
Cimex lectularius	" 1 layer " "	30	90
Cimex lectularius	" 2 layers " "	8	90
Cimex lectularius	Exposed on vertical paper	90	100

(3) Residual insecticidal effects, smokes of γ-BHC and DDT: Kill of certain insects at various time periods after the exposure of tested surfaces to smoke deposit: 426

Surface	Insecticide	Exposure (hrs)	% Mortality Of Cimex lectularius (on surfaces with deposits of stated age) 1 day	1 week	1 month	6 months
Horizontal	DDT	6	55	86		77
"	"	17	100	100	100	75
"	"	24	100	100	95	94
"	γ-BHC	6	87	72	—	—
"	"	17	98	89	26	—
"	"	24	100	97	5	—

(3) Residual insecticidal effects, smokes of γ-BHC, and DDT: Kill of certain insects at various time periods after the exposure of tested surfaces to smoke deposit: 426

Surface	Insecticide	Exposure (hrs)	% Mortality of Cimex lectularius (on surfaces with deposits of stated age)			
			1 day	1 week	1 month	6 months
Vertical	DDT	6	4	24	—	5
"	"	17	33	52	11	28
"	"	24	36	47	22	6
"	γ-BHC	6	27	8	—	—
"	"	17	45	12	12	—
"	"	24	84	22	11	—

Surface	Insecticide	Exposure (hrs)	% Mortality After Exposure To Surfaces Treated 1 Week Before Test	
			Aëdes aegypti	Culex molestus
"	DDT	3	57	—
"	"	6	100	67
"	"	17	100	100
"	γ-BHC	3	100	—
"	"	6	100	100
"	"	17	100	100
Inverted	DDT	3	17	—
"	"	6	96	13
"	"	17	88	98
"	γ-BHC	3	94	—
"	"	6	100	95
"	"	17	100	100

(4) Estimated deposits mg/ft², space 2500 ft³ (70m³), 1 smoke grenade/test. Grenades containing 110g crude DDT (70% p,p' -DDT); 120g crude BHC (10-12% γ-isomer) 60-70% DDT, BHC emitted undecomposed as particles <1 μ in diameter: 426

Hgt From Floor	DDT Collecting Paper 2 Tests			γ-BHC Collecting Paper 1 Test		
	Horizontal	Vertical	Inverted	Horizontal	Vertical	Inverted
9-11 ft	20.4, 25.7	3.8, 5.9	3.9, 5.5	30.9	10.1	6.0
6-7 ft	13.0, 14,8	3.9, 8.5	3.9, 4.4	17.3	3.0	2.1
3-4 ft	14.0, 18.5	3.2	3.2	19.5	—	—

8) BHC, as dusts, in the control of certain cotton plant insects:

a) Cage tests: insects placed on dusted plants at stated time period after treatment: [Ref. 2979]

Insect	γ-Isomer (%)	Time After Dusting (hrs)	Net Kill %
Chlorocroa sayi	1	28	75
" "	2	8	85
" "	10	19-43	100
Euschistus impictiventris	2	8-28	95
	10	19-43	100
Lygus spp	5	3	100
Creontiades femoralis	5	15	100

b) Cotton flea hopper: Insecticide application at rate of 16 lbs/acre as dusts: [Ref. 1661]

Insecticide	Concentration (% active ingredient)	% Kill in 24 Hrs
BHC	10	100
"	5	100
"	2.5	98-100
"	1.25	93-100
"	1	86
"	.62	92
"	.31	83
"	.3	58
"	.1	30
"	.03	18
"	.01	18
DDT-pyrophyllite	5	61
DDT-sulfur	4.6 (DDT)	95-100
Pyrophyllite control		0

9) Comparative toxicity BHC and other insecticides:

a) Toxicity of BHC and DDT as dusts and sprays on foliage 300

Insect	Feeding		Concentration (%)	Deposit (μg/cm²)		% Mortality (3 days)	
	BHC	DDT		BHC	DDT	BHC	DDT
				Dusts			
Phlyctaenia rubigallis	much	slight	0.5	95	95	0	79
Prodenia eridania	slight	slight	0.5	110	110	96	17
Oncopeltus fasciatus	—	—	1.0	125	125	75	17

Insect	Feeding		Concentration (%)	Deposit (μg/cm²)		% Mortality (3 days)	
	BHC	DDT		BHC	DDT	BHC	DDT
				Dusts			
Diaphania hyalinata	moderate	much	0.1	115	115	100	54
Pachyzancla bipunctalis	moderate	much	0.1	95	95	100	67
Altica bimarginata	0	0	2.0	140	255	100	75
Pieris rapae	moderate	much	0.1	110	125	96	75
Cirphis unipuncta	moderate	moderate	0.5	85	115	88	71
Heliothis armigera	much	much	0.5	140	140	42	33
Peridroma margaritosa	moderate	moderate	0.5	95	85	83	92
				Sprays			
Pieris rapae	moderate	much	.002	—	—	96	13
Prodenia eridania	much	much	.01	—	—	58	29
Pachyzancla bipunctalis	much	much	.002	—	—	67	54
Diaphania hyalinata	much	much	.002	—	—	79	96

b) Toxicity, as dusts, for larvae of Aëdes aegypti, BHC and others: 2848

Insecticide	Lbs/Acre	% Mortality After		
		1 day	2 days	3 days
BHC (crude)	0.5	0	23	93
" "	0.06	0	0	20
BHC (γ-isomer)	0.5	0	97	100
" "	0.06	0	33	80
DDT	0.5	0	43	97
"	0.06	0	23	47
Cuprous cyanide	0.5	47	73	87
" "	0.06	30	40	65

c) Toxicity, BHC and others, in poison baits for Locusta migratoria, laboratory tests: 2848

Insecticide	Concentration (%)	% Mortality, 48 hrs
BHC (crude 10-12% γ-isomer)	0.02	62
" (" " ")	0.05	96
Sodium arsenite	4.0	66
DDT	0.2	57

d) Comparative LD_{50} values, BHC and others: Melanoplus femur-rubrum: 3266,1756

Insecticide	Route	LD_{50} (mg/g)	Remarks
BHC (37% γ-isomer)	contact	0.011-0.013	At >.0129 mg/g 3 of 41 lived >2 days; at <.112 mg/g 5 of 22 died before 7 days.
BHC (37% γ-isomer)	or	ca0.035	Death within 1-2 days.
BHC (pure γ-isomer)	or	0.005-0.01	
Chlordane	contact	0.0195-0.022	At >.0218 mg/g 3 of 32 lived >4 days; at <.0195 mg/g 11 of 40 died before 4 days.
Chlordane	or	ca0.014	Death within 1-2 days.
Chlordane	or	0.0125-0.025	
DDT	contact	>1.635	
DDT	or	>0.26	
Toxaphene	contact	>0.75	
Toxaphene	or	0.086-0.105	Death at end of 48 hours.

e) Toxicity, BHC, other chlorinated hydrocarbons, for Melanoplus femur-rubrum nymphs; field plot tests on alfalfa plantings: 3266

Insecticide	Rate Actual Toxicant (lbs/acre)	Insects Caged On Plots Before Treatment		Insects Caged On Plots 30 Min After Treatment	
		(days)	(% Kill)	(days)	(% Kill)
γ-BHC (1% dust)	0.15	1	89.2	7	10.1
" " "	"	2	95.6	—	—
" " "	0.3	1	84.5	4	5
" " "	"	2	91.0	7	20
" " (0.5% dust)	0.15	1	72.6	7	11.3
" " " "	"	2	83.4	—	—
" " " "	"	4	91.4	—	—
" " " "	"	5	92.0	—	—
" " " "	"	7	93.1	—	—
" " " "	0.3	1	88.7	3	14.3
" " " "	"	2	94.0	—	—
				2	4.9
Chlordane (2% dust)	1.0	1	73.1	4	66.0

e) Toxicity, BHC, other chlorinated hydrocarbons, for Melanoplus femur-rubrum nymphs; field plot tests on alfalfa plantings: 3266

Insecticide	Rate Actual Toxicant (lbs/acre)	Insects Caged On Plots Before Treatment (days)	(% Kill)	Insects Caged On Plots 30 Min After Treatment (days)	(% Kill)
				5	83.5
Chlordane (2% dust)	1.0	2	98.1	7	93.2
" "	0.5	1	32.5	2	8.5
" "	"	2	62.5	7	36.6
" "	"	4	66.3	—	—
Toxaphene (2% dust)	1.0	4	73.1	5	19.7
γ-BHC (5.75% wet. pwdr)	0.173	—	—	7	31.1
Chlordane (50% wet. pwdr.)	1.0	—	—	7	31.1
				2	8.2
Toxaphene (25% wet. pwdr.)	3.0	—	—	4	78.1
" " "		—	—	5	83.6
" " "		—	—	7	91.8
BHC (10% γ) 20% + xylene 70%	0.075	2	40	5	5.2
+ Atlox 1045A 10% w/w	"	3	72.3	—	—
" "	"	5	80	—	—
" "	0.15	2	54.9	5	13.5
" "	"	3	71.4	—	—
" "	"	5	78.0	—	—
" "	0.3	1	100	6	7.4
BHC (10% γ) 20% + dioxane 70% +					
Atlox 1045A 10% w/w	0.3	1	100	6	23.3
Chlordane 62% + xylene 33% + Atlox	.5	5	59.8	5	42
5% " "	1.0	1	62.9	6	78.8
" " "	"	2	95.9	—	—
Toxaphene 50% emulsion w/w	3.0	1	62	3	22.2
				4	31.1
" " "		2	92	6	61.1
Control		7	2.2	—	—

f) Effectiveness of BHC and other insecticides applied as dusts vs. various cotton plant insects. 1661

Insecticide	Concentration (% active ingredient)	Dosage (lbs/acre)	% Mortality After 1 day	3 days	5 days
			Boll Weevil (Adult)		
BHC	10	32	34	86	95
"	"	16	25	73	88
"	"	8	20	64	79
Calcium arsenate		8	6	35	70
			Cotton Leafworm (3rd Instar)		
BHC	10	32	83	100	100
"	"	16	80	99	100
"	"	8	56	96	98
"	5	8	14	65	73
"	2.5	8	4	40	44
"	1.25	8	5	28	35
Calcium arsenate		8	32	93	96
			Bollworm (3rd Instar)		
BHC	10	32	14	58	70
"	"	16	11	31	39
"	"	8	6	29	32
DDT-pyrophyllite	5	16	26	85	97
Calcium arsenate		16	19	64	85
			Tarnished Plant Bug (Adult)		
BHC	10	32	100	100	100
"	5	8	100	100	100
"	2.5	8	69	100	100
"	1.25	8	71	100	100
"	0.62	8	62	85	92
DDT-sulfur	4.6 (DDT)	5	100	100	100
			Tarnished Plant Bug (Nymphs)		
BHC	5	16	45	100	100
"	1.25	16	23	85	100
			Southern Green Stinkbug (Adult)		
BHC	10	32	48	64	68
"	"	16	23	59	59

Insecticide	Concentration (% active ingredient)	Dosage (lbs/acre)	% Mortality After 1 day	3 days	5 days
			Southern Green Stinkbug (Adult)		
BHC	10	8	16	38	47
DDT-pyrophyllite	10	10	7	37	63
			Southern Green Stinkbug (2nd Instar)		
BHC	10	32	71	90	95
"	"	16	28	66	86
"	"	8	19	73	88
DDT-pyrophyllite	10	16	17	100	100
			Southern Green Stinkbug (5th Instar)		
BHC	10	32	9	14	14
"	"	16	12	23	31
"	"	8	4	4	4
DDT-pyrophyllite	10	16	0	0	13

g) Toxicity of BHC and other insecticides vs Blattella germanica. Application: As dusts; 80-150 insects/trial; tests considered complete 48 hrs after no additional dead or moribund individuals were present: 2357

Insecticide	Roaches Dusted at µg/cm^2	Av. % Killed, Moribund	Container Dusted Conc.	at µg/cm^2	Av. % Killed, Moribund
BHC (5% γ)	0.5	28.7	0.1% γ	0.125	7.0
" "	0.75	45.3	"	0.25	69.7
" "	1.0	92.5	"	0.5	98.7
DDT (10% dust)	15.0	50.0	0.5% dust	2.0	30.0
" "	20.0	64.3	"	2.5	46.0
" "	20.5	90.0	"	3.0	74.3
Chlordane (5% dust)	1.0	34.1	0.5% dust	0.25	14.3
" "	2.0	52.5	"	0.5	35.2
" "	3.0	87.0	"	0.75	90.0
Sodium fluoride (25%)	104.19	24.0		30	39.0
" " (pure)	148.8	57.3		40	51.0
" " (")	223.2	70.0		50	95.0

h) Toxicity of BHC and other insecticides vs. Blattella germanica. As Minimum Effective Deposit* in mg/1000cm^2 (930cm^2 = 1 ft^2). Deposits made by evaporation from acetone solutions on glass surface. *MED measured as the minimum deposit producing maximum degree of paralysis: 1367

Insecticide	MED (mg/1000cm^2)	Remarks
BHC	0.1-0.5	Little difference in rate of paralysis between .5-3.5 mg/1000cm^2.
Chlordane	0.5-1.0	Little difference in paralysis between 1.0, 5.0, 10.0 mg/1000 cm^2.
DDT	10.0-25.0	Little difference in paralysis between 25, 40,80 mg/1000cm^2.
	Minimum Exposure Time For Maximum Paralysis	
BHC	10 min at 0.5 mg/1000cm^2	CO$_2$ anesthesia enhanced paralysis as compared with free running exposures.
Chlordane	12-20 min at 1 mg/1000cm^2	Mobility and immobility on treated surface gave no significant difference.
DDT	1 hr at 25 mg/1000cm^2	Mobility and immobility on treated surface gave no significant difference.
Toxaphene	> 1 hr	

1367

i) Comparison of toxicity of BHC (γ-isomer) and several chlorinated hydrocarbon insecticides vs. Musca domestica and Aëdes aegypti as sprays and residues: 1094

(1) Sprays

Insecticide	% KD$_{30}$ Min At 0.25%	0.5%	1%	2%	5%	% Kill In 24 Hrs At 0.25%	0.5%	1%	2%	5%	LC$_{90}$ (%)
					For Aëdes aegypti (adult)						
γ-BHC	3	18	37	91	99	74	95	99	99	100	0.4
DDT	0	3	1	4	22	34	88	88	97	100	1.0
Chlordane	0	0.3	1	1	15	17	23	35	90	99	2.96
Toxaphene	0	0.1	0.1	0.2	2	16	21	27	42	72	29.26
					For Musca domestica (adult)						
γ-BHC	54	76	95	99	100	93	99	100	100	100	.17
DDT	0	10	9	56	71	34	85	84	98	99	1.01
Chlordane	0	0	0	0	8	54	66	87	99	100	.88
Toxaphene	0	0	0	0.4	10	11	14	41	59	94	4.89

(2) Residues

Insecticide	% Mortality (24 hr) after 2 Hr Exposure To Residues At 10 mg/ft²					
	Age of Residue					
	1 week		4 weeks		8 weeks	
	A. aegypti	M. domestica	A. aegypti	M. domestica	A. aegypti	M. domestica
BHC (tech.)	100	63	49	16	33	21
Chlordane	99	94	47	59	24	66
DDT	99	73	46	50	56	36
Toxaphene	41	8	14	1	20	0

(3) Number of weeks during which stated deposits (mg/ft²) retained ability to produce 90% kill or KD:

Insecticide	Deposit (mg/ft²)															
	50		100		200		400		50		100		200		400	
	Kill	KD	Kill	KD	Kill	KD	Kill	KD	Kill	KD	Kill	KD	Kill	KD	Kill	KD
	Musca domestica								Aëdes aegypti							
BHC (tech.)	0	1	0	1	9	8	9	12	9	4	9	8	9	8	24	20
Chlordane	9	1	13	1	28	1	36+	1	13	1	13	1	28	8	32	20
DDT	36+	36+	36+	36+	36+	36+	36+	36+	36+	20	36+	20	36+	24	36+	36+
Toxaphene	0	1	9	1	24	1	28	1	5	0	9	0	36+	1	36+	1

(4) % Mortality in 24 hours after 2 hour exposures on surfaces holding the stated deposits in mg/ft²; Anopheles quadrimaculatus = I; Aëdes aegypti = II: 1094

Insecticide	Deposits In mg/ft²							
	50		100		200		400	
	% Mortality							
	I	II	I	II	I	II	I	II
BHC (tech)	7	8	5	12	12	18	54	33
Chlordane	25	25	48	20	66	42	96	81
DDT	85	92	96	95	98	100	100	100
Toxaphene	21	11	31	20	93	51	98	84

j) Persistence (residual effect), in soil, of BHC (γ-isomer) measured against Anomala orientalis, and compared with DDT: 2726

Insecticide	Dosage (lbs/acre)	% Mortality After					
		Immediately After Treatment	5 months	8 months	19 months	23 months	26 months
γ-BHC	0.75	44.2	—	—	—	—	—
	1.5	36.8	—	—	—	—	—
	3.0	69.5	—	—	—	—	—
	4.5	98.0	—	—	71.5	—	—
	7.5	100	—	—	92.0	—	—
	12.0	100	—	—	99	—	—
	15.0	100	—	—	100	—	—
	30.0	100	—	—	100	—	—
	60.0	100	—	—	100	—	—
DDT	25.0	91	—	86.1	—	—	40
	50.0	100	—	95.6	—	—	50
	100.0	100	—	97.9	—	—	75.3
	25.0	—	83.7	—	—	45.8	—
	50.0	—	95.1	—	—	59.5	—

k) Comparison of effectiveness of BHC and other insecticides vs. Melolontha melolontha: (For M. melolontha DDT is ineffective.) 3184

Insecticide	By Contact (µg/insect)		Relative Toxicity At	
	LD_{50} 5 days	LD_{80} 5 days	LD_{50}	LD_{80}
BHC (tech)	0.7	2.5	1	1
Dieldrin	1.6	5	0.4	0.5
Aldrin	2.7	>6	0.25	<0.4
Chlordane	9	20	0.08	0.12
Toxaphene	ca7	ca20	ca0.1	ca0.12

l) Comparative toxicities of BHC and other insecticides vs. 1st and 2nd instar nymphs of Melanoplus differentialis. Used as contact emulsion sprays prepared from miscible oil concentrates: 1102

1102

Insecticide	LD_{50} (lbs/acre)
BHC	0.04
Dieldrin	0.03
Aldrin	0.04
Parathion	0.05
Lindane (γ-BHC)	0.08
Chlordane	.49
Toxaphene	.91

m) BHC and other insecticides in the control of Psylla pyri. As autumn sprays vs. the last larvae of the season and hibernating adults (and incidentally, aphid sexual stages). Entomophagous and predatory insects unharmed. Treatment applied in 1st half of October by motor spraying at a pressure of 12k/cm^2. Conditions: France at Versailles. 2275

Insecticide	Dilution%	Coefficient Of Efficacity
BHC (12% γ)	0.3	98.7
White summer oil	1.5	14.9
" " " + nicotine 11.5%	0.75	31.9
" " " + rotenone 0.9%	1.0	56.6
DDT (emulsion 20% active ingredients)	0.5	27.7
SPC (emulsion 20% active ingredients)	0.35	74.1
TEPP (13% active ingredients)	0.15	12.8
Parathion (emulsion 3% active)	0.75	100
" (" 4% ")	0.35	98.7
" (1.5% active + white oil)	1.0	96.1
" (suspension 3% active)	0.35	100

n) BHC and other insecticides compared by field tests (corn fields) in the control of Sphenarium purpurascens: 307

Insecticide	Concentration	Active Ingredients (lbs/acre)	% Mortality After	
			12 hours	24 hours
BHC	1% dust	0.36	86.6 (78-92)	94.2 (90-97)
"	2.5% "	0.85	93 (89-98)	97 (93-100)
Dieldrin	1% "	0.35	74.2 (68-80)	98.2 (96-100)
"	2.5% "	0.88	89.8 (87-93)	99.8 (99-100)
Aldrin	1% "	0.32	77.8 (69-88)	97.8 (95-100)
"	2.5% "	0.82	88.6 (83-96)	99.6 (99-100)
Isodrin	0.5% Spray	0.43	83.2 (81-92)	91.4 (80-86)
Parathion	0.5% dust	0.16	43.6 (36-51)	69.4 (61-80)
"	1.0% "	0.35	66.8 (59-80)	76 (69-84)
Toxaphene	5% "	1.74	26.8 (18-36)	53 (46-60)
"	10% "	3.6	40.4 (36-47)	61.4 (55-69)
Chlordane	2.5% "	0.95	32 (27-39)	46.6 (41-54)
"	5% "	1.8	49.6 (39-62)	63.8 (50-77)
Endrin	0.5% spray	0.36	32.8 (24-40)	47.6 (43-59)

o) Comparative toxicity of some chlorinated hydrocarbons for Anthonomus grandis: 2276

Insecticide	Food Plant Dusted (combined contact, stomach toxicity) LD_{50} (% active ingredient as lbs/acre)	Insect Dusted (contact action) LD_{50} (% active ingredient as lbs/acre)	Fumigant Action LC_{50} (mg active ingredient per liter)
BHC (tech.)	1.0	3.7	47.6; 59.2
α "	—	—	467.3
β "	—	—	1213.0
γ "	—	—	233.5
δ "	—	—	778.2
Dieldrin	0.9	2.7	16.6
Aldrin	1.1	6.6	12.9
Chlordane	10.1	—	21.9
Toxaphene	6.4	—	—
DDT	9.1	—	—
1,1-Bis(p-chlorophenyl)-2-nitro-	—	—	—
propane (tech.)	11.4	—	—
1,1-Bis(p-chlorophenyl)-2-nitro-	—	—	—
butane (tech.)	16.7	—	—

p) BHC and other insecticides in the control of cabbage caterpillars, Pieris rapae and Trichoplusia ni in 2 successive years. Field tests. Pieris rapae predominant in year I, Trichoplusia ni in year II. Application of insecticides as dusts. Difference for significance: At 5% level yr I = 11.4, yr II = 14.0, at 1% level, I = 16.4, II = 18.6. 796

Insecticide	Concentration Of Dust (%)	Year I % Control	Year II % Control
γ-BHC	0.38	84.2	—
γ-BHC	1	—	62.7
DDT	1	—	81.9
"	2	87.5	87.5
"	3	88.9	87.6
DDD	3	—	87.0
Methoxychlor	3	—	60.9
Chlordane	3	—	72.6
Toxaphene	3	—	80.8
Rotenone	0.75	85.8	35.5
Ryania	30	83.1	—
"	40	—	46.0
Sabadilla (seed)	10	84.5	—
Pyrethrum	20	78.6	—
Pb arsenate	20	77.6	—
Ca arsenate	20	—	0
Zn fluorarsenate	20	26	—
2-Mercapto-6-nitrobenzothiazole	10	3.8	0

q) BHC and other insecticides as baits in sugar and molasses solutions to control flies (Musca domestica). Laboratory and field evaluations: 1915

Insecticide	Laboratory Tests (% down or dead in)			Field Tests (Degree Of Control)
	30 min	1 hr	24 hrs	
BHC (1%) tech.	43	76	100	—
γ-BHC (1%)	3	6	100	unsatisfactory
Aldrin (1%)	20	76	100	—
Bayer L 13/59 (0.1%)	54.5	56.5	100	excellent
Chlordane (1%)	10	20	100	—
Chlorobenzilate (1%)	0	0	60	—
DDT (1%)	30	44	98	unsatisfactory
CS-708 (1%)	13	20	80	fair
Diazinon (1%)	23	36	90	excellent
Dieldrin (1%)	20	66	100	unsatisfactory
Heptachlor (1%)	6	48	100	"
Lethane 384 (1%)	0	0	0	—
Malathion (1%)	43	56	93	excellent
Metacide (1%)	23	23	100	—
Methoxychlor (2%)	23	20	93	unsatisfactory
NPD (1%)	36	40	90	—
Parathion (1%)	13	13	90	—
Strobane (1%)	10	36	96	—
TEPP (.5%)	53	56	100	—
Toxaphene (1%)	40	56	100	unsatisfactory
Borax (saturated)	0	0	33	—
Boric acid (.63%)	3	3	50	—
Copper sulfate (2%)	0	0	36	—
Formalin (2%)	16	16	30	—
Cryolite (1%)	0	0	0	—
Sodium fluoride (2.5%)	0	0	66	—
Rotenone (1.3%)	0	0	50	—

10) BHC vs. beneficial and useful insects:

a) Use of BHC on cotton has enhanced infestations of phytophagous mites (Tetranychus spp.) and on citrus has enhanced Paratetranychus citri infestation by destroying or thinning out "populations" of beneficial insect predators. 353

b) Effect of BHC on the honeybee, Apis mellifera, and other bees: 535,3247

(1) Dusting inside of hives of Apis indica with 1% BHC gave complete mortality in 6 days; 6% dust gave complete mortality in 10 hrs. $\frac{1}{4}$ oz. of BHC treated honey (0.05% BHC) gave 24% mortality in 6 days with subsequent gradual disappearance from the hive of the remaining bees.

(2) Concentrations of γ-BHC and DDT in commercial sprays required to give 20, 50 and 95% mortality of Apis mellifera by contact poisoning: As g dispersible powder/100cc H_2O.

	LC_{20}	LC_{50}	LC_{95}
BHC (P530 spray)	.00089	.0014	.0032
DDT (Guesarol E spray)	.1	.16	.39

(3) % Mortality on 1st and 5th days of Apis mellifera workers exposed to γ-BHC and DDT spray films on glass cage walls. Films derived from commercial preparations:

	Concentration Spray (%)	% Mortality On	
		1st day	5th day
BHC, P530 spray (as γ-BHC)	0.0065	100	—
	0.0032	100	—
	0.0016	30	33
	0.0004	3	10
control	—	0	3
DDT, Guesarol E spray	1.0	100	—
	0.5	93	100
	0.2	37	67
	0.1	13	37
control	—	5	15

(4) As stomach poisons: γ-BHC and other insecticides, as suspensions in suitable media:

Substance	Lethal Dose (mg x 10^{-3}/bee) To Give Mortality Of		
	20%	50%	95%
γ-BHC (3rd day)	.03	.08	.54
DDT (" ")	5.4	9.1	25.0
Lead arsenate (3rd day)	32.0	86.0	610.0
" " (5th day)	6.1	20.0	210.0

(5) % Mortality of adult Apis mellifera on the day following exposure to blooms of plants sprayed with BHC and DDT:

Treatment	% Active Agent	% Kill On		
		Apple	Cineraria sp.	Michaelmas daisy
DDT, Guesarol E spray	1	0	—	4
" " " "	.5	—	0	4
" " " "	.2	—	0	—
" Guesarol dust	5	0	—	—
BHC, P530 spray (as γ-BHC)	.1	100	100	100
" " " "	.052	52	69	80
" " " "	.039	—	—	70
" " " "	.026	0	0	100
" " " "	.012	—	9	—
" " " "	.0065	—	0	—
BHC, PP flea beetle dust	.2	—	—	100
control		0	0	0

(6) Speed of toxic action of BHC vs. Apis mellifera workers. Length of time after treatment before appearance of slightly affected and moribund individuals:

	% γ-Isomer	Min. For Slightly affected	Min. For Moribund	Min. For 100% Kill
BHC (P530 spray)	.21	15	30	180
" " "	.1	45	105	195
" " "	.052	60	135	—
" " "	.039	75	150	—
" " "	.026	75	180	—
BHC (PP flea beetle dust)	.2	60	135	—

(7) % Mortality of Apis mellifera adult workers caused by 1-4 day old films of BHC (P350 spray) on open blossoms:

Days After Spraying	Apple				Michaelmas Daisy	
	10%-γ-BHC		.052% γ-BHC		0.052% γ-BHC	
	% Mortality					
	treated	control	treated	control	treated	control
0	100	0	63	0	79	15
1	57	0	64	0	57	15
2	—	—	44	0	40	5
3	33	0	—	—	27	0
4	—	—	18	0	3	10

(8) Under field conditions Apis mellifera workers may be killed by contact of ca 1 minute with open BHC-treated flowers. Returns of marked bees to BHC-treated plots, over a period of days, was always significantly less than that of controls.

(a) BHC is highly toxic (DDT relatively non-toxic) to Bombus pratorum, Andrena spp., Osmia rufa (bumble bees). In Bombus terrestris and B. agrorum the susceptibility of workers to BHC is comparable to that of Apis mellifera; queens and drones are more resistant to BHC than workers (resistance to DDT is very marked).

(b) The foregoing fact is important since in spring, when fruit blossom is sprayed, the working Bombus "population" is represented almost wholly by queens essential for the maintenance of the species.

(c) BHC, on open blossom, appears to have no repellency for bees.

(d) The speed of toxic action of BHC does not prevent return of exposed individuals to the hive, with consequent danger to other bees in the hive (nurse bees particularly) from contaminated pollen and nectar.

(e) Bees from BHC affected colonies are said to become "furiously mean." 3099

PHARMACOLOGY, BIOCHEMISTRY, SYMPTOMATOLOGY, BIOLOGICAL AND PHYSIOLOGICAL ACTIVITY; INSECTS

1) Studies have been directed largely to the γ-isomer on the general assumption that the principal activity of BHC is due to this substance. The γ-isomer is several 100 times more toxic to insects than the other isomers. 846

2) The toxic symptoms in insects are essentially DDT-like but with a more rapid onset. This does not neces- 353
sarily indicate that the mechanism of action is identical for BHC and DDT. Both may be characterized as 2231
neurotoxic agents. 2538
a) The primary site of action appears to be the posterior nervous system. 3096

3) Symptoms of BHC poisoning in insects; physiological activity:

a) In the desert locust Schistocerca: 2458

(1) Prodromal phase: Abdomen raised. (2) Typical phase: Telescopic abdominal movements, abdomen rubbed by hind legs. (3) Choreo-atoxic phase: Hyperexcitability to stimulus, attempts to fly, uncoordinated movement. (4) Clonic phase: Tremors of legs, wings, mouth parts, abdomen distended. (5) Paralytic phase: Progressive cessation of movement; insects may copulate before coma.

b) In Periplaneta americana: 2744

(1) Tremors followed by ataxia, convulsions, falling, finally passing into prostration, paralysis, death. (Development of symptoms more rapid than with DDT but in other respects almost identical.)

c) In Blattella germanica: 1441

(1) Dusted with γ-isomer the insect shows: Excitement, tremors, convulsions, passing over to paralysis in 20-40 minutes, with death in a few hours.

d) In Musca domestica: 353

(1) Rapid development of the convulsive phase followed by paralysis and death.

e) Effect on respiration:

(1) γ-Isomer stimulates respiration (as does DDT) in Oryzaephilus surinamensis. 2040,2041

(2) Blattella germanica, injected with 1 μg γ-isomer: Immediate increase in respiratory rate, O_2 uptake, after 60 minutes (in period of spasm and convulsion) reached 5 times the normal level. Topical application by spraying yielded the same effects. 1441

f) Other physiological effects:

(1) γ-Isomer by injection in Periplaneta americana at 100 $\mu g/g$ had slight effect on heartrate but gave irregularity of pulsation. 2421

(2) Topical application of γ-isomer to legs of Periplaneta americana: After ca 1 hour action potential responses in bursts of 2-4 repetitive spikes may be recorded from the crural nerves at $\frac{1}{2}$ second intervals. May be distinguished from action potential responses to DDT. 520

(a) γ-Isomer does not stimulate motor nerves in Periplaneta americana (or in Calliphora erythrocephala) but acts on the ganglia; an intact reflex arc is necessary for manifestation of characteristic tremors and twitches. 295

(3) In Periplaneta americana, prostrate from γ-BHC poisoning, ventral nerve cord acetylcholine was increased from a normal 38 μg/cord to 57 μg/cord. (DDT produced a like increase.) 3096

g) Metabolism of BHC:

(1) Of a 0.3 μg dose by injection in Musca domestica, 23% was metabolized in 2 hours, 32% in 4 hours with no further destruction. In BHC resistant strains metabolism was more rapid. 2415

(2) An anti-metabolite theory of action for the γ-Isomer has been elaborated, and γ-BHC is looked upon as a metabolic competitor of meso-inositol. Evidence in support of the theory is conflicting. 2848
2186,
1817,411,1077,528,506,1004,2227,3087,846,2945

h) Cytological effects:

(1) Accumulation and clumping, of lipoid globules in fat cells and ganglia. Nucleolar changes in cell nuclei of the hypodermis. 2944

i) Entry of BHC in the insect body:

(1) Passage across the intact integument of insects is manifested by the intense contact toxicity of BHC 2744
and by close agreement between the LD_{50} in topical and injection application in some insects. 846
(a) In Periplaneta americana LD_{50} topical = 5 $\mu g/g$, injection = 4 $\mu g/g$.

(b) Attribution of toxic effects to the γ-isomer rests on much evidence similar to the following: LD_{50} (by intra-abdominal injection) for Periplaneta americana = 17 $\mu g/g$ while 85 $\mu g/g$ α-, β- isomers, by the same route and in a dosage close to their solubility limits, have no effect. 846

(2) Penetration of BHC isomers through the cuticle of *Sitophilus granarius* (absorption by contact with residues on paper in exposures of 7-12 hrs) appears to be proportional to their solubility in cuticular wax. The γ-isomer enters in a given time in far the greater amount. 114
   (a) Solubility in g/100g in cuticular wax: $\alpha = 1.7$, $\beta = .4$, $\gamma = 8.7$, $\delta = 14.8$.
   (b) Amount appearing in insect after 7-12 hr exposure to residues, 11μg/cm^2 on paper: In exterior wax: $\alpha = 12\mu$g/g insect, $\beta = \mu$g/g insect, $\gamma = 60\mu$g/g insect, $\delta = 102\mu$g/g insect. In the insect interior: $\alpha = 4\mu$g/g insect, $\beta = 4\mu$g/g insect, $\gamma = 43\mu$g/g insect, $\delta = 8\mu$g/g insect.

(3) Transport, once entry into the insect body has been gained, is principally via the circulating haemolymph, and secondarily via nerve tissue. 295
   (a) Elimination from the insect body is via the Malpighian tubules.

RESISTANCE DEVELOPED TO BHC: (Also see the general treatment of resistance.)

1) Development of tolerance, on exposure to BHC, or as cross-tolerance in strains exposed to other chlorinated hydrocarbon insecticides, has been noted in *Musca*, *Blattella*, *Pediculus*, *Anopheles*, *Boöphilus*. 352
   a) A stock of *Musca domestica*, reared through 28 generations in a BHC contaminated laboratory, showed a 6% mortality on exposure to γ-isomer concentrations which once produced 40% mortality in the ancestors of the line. 353
   b) Resistant stocks of *Musca* have been collected under field conditions from heavily treated sites. 353

SCREENING TESTS

1) Results of extensive screening tests of tech. BHC and its individual isomers under various conditions, and with various insects and related arthropods, may be found in Ref. 1801.

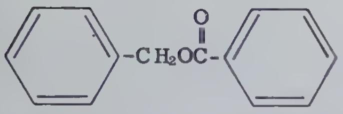
ECONOMIC CONTROL OF INSECTS WITH BHC: Reports of use against various insects.

1) Vs. *Melanoplus* spp., 95-98% control at 0.5 lb/acre. 334,1531
2) " " ", 98% control at 2.5 lb/acre. 2028
3) Vs. *Aphthona virescens*, 100% control with 10% dusts in 12 hours. 873
4) Vs. *Melanoplus* spp., 100% kill with suspensions of a product containing 12% γ-isomer. 1242
5) Vs. *Nezara viridula*. 1099
6) Vs. *Euschistus tristigmus*. 3368
7) Vs. *Anasa tristis*. 3222
8) Vs. *Oncopeltus fasciatus*. 356
9) Vs. *Lygus oblineatus*; relatively ineffective.* 515
10) Vs. Cotton Mirids. 74
11) Vs. *Psallus seriatus*, 10% BHC dust controls. 2438
12) Vs. *Rhipicephalus appendiculatus*. 3330
13) Vs. *Ornithodorus moubata*. 2514
14) Vs. *Ornithodorus megnini*. 2841
15) Vs. *Lasius americanus*, 0.3% suspension on turf → 60% control. 1780
16) Vs. *Damalinia bovis*, *D. canis* 1% dusts → complete control. 3066,2980
17) Vs. *Haematopinus eurysternus* 0.3% suspension, as a dip, controls. 1084
18) Vs. *Linognathus setosus*. 2980
19) Vs. *Aëdes taeniorhynchus*, 0.2-0.4 lb/acre tech BHC (12%γ) controls DDT resistant strains. 1802
20) Vs. Mosquitoes; on clay walls may be superior to DDT. 671
21) Vs. *Lucilia cuprina*. 2804
22) Vs. *Hypodermia bovis* and *H. lineatum*, effective as salves, not as sprays. 1086
23) Vs. *Gastrophilus* spp (larvae), ineffective.* 2980
24) Vs. *Sitophilus oryzae* and *Rhizopertha dominica*, highly effective but taints products. 1129
25) Vs. *Tenebrio* and *Ephestia* larvae: Resistant to BHC. 353
26) Vs. *Philaenus leucophthalmus*. 2465,511
27) Vs. *Tomaspis saccharina* and *T. flavilatera*. 1673,2503
28) Vs. *Empoasca fabae*: Ineffective* 3016
29) Vs. *Psylla pyricola*: Not as effective as rotenone. 74
30) Vs. *Aphids*: Although superior to DDT, not the insecticide of choice. 353
31) Vs. *Pseudococcus maritimus*: Gives only 50-83% control. 2356
32) Vs. *Taeniothrips* spp. 2871,2554
33) Vs. *Thrips tabaci*. 2403,1555
34) Vs. *Scirtothrips signipennis*. 2905
35) Vs. *Pieris rapae*. 2457
36) Vs. *Estigmene acraea*: Ineffective.* 91
37) Vs. *Anticarsia gemmatilis*. 110,1873
38) Vs. *Alabama argillacea*. 91
39) Vs. *Laphygma* spp. 349
40) Vs. *Cirphis unipuncta* 300
41) Vs. *Prodenia eridania*. 3016
42) Vs. *Tortrix pronubana*: Does not give complete control. 2554
43) Vs. *Polychrosis viteana*: Ineffective.* 624
44) Vs. *Laspeyresia nigricana*: Ineffective.* 3375

45) Vs. Carpocapsa pomonella: Inferior to DDT, taints fruit.	74,248,3263
46) Vs. Diaphania hyalinata.	2226
47) Vs. Phlyctaenia rubigallis.	300
48) Vs. Diatrea saccharalis.	248
49) Vs. Gnorimoschema operculella Ineffective.*	353
50) Vs. Clysia ambiguella: Ineffective.*	1104
51) Vs. Pectinophora gossypiella.	2677
52) Vs. Thyridopteryx ephemeraeformis: Poor control.	353
53) Vs. Profenusa canadensis.	1360
54) Vs. Vespula and Polistes	832
55) Vs. Hylemyia brassicae and H. floralis	3016,659
56) Vs. Psylla rosae.	2378
57) Vs. Anastrephia ludens: Inferior to others in control of.	42
58) Vs. Liriomyza orboni: Mediocre; gives up to 66% control only.	1913,2145
59) Vs. Monarthropalpus buxi: Incomplete control with 0.3% spray.	2960
60) Vs. Epilachna varivestis: Relatively ineffective.*	2403,323
61) Vs. Ludius spp.: Control at 2 lb/acre.	2530
62) Vs. Agriotes mancus: Control at 1 lb/acre and 0.25 lb/acre.	2470,1269
63) Vs. wireworms: Control at 0.2 lbs/acre.	112
64) Vs. Ctenicera aereipennis destructor.	871
65) Vs. Horistonotus uhleri.	91
66) Vs. Popillia japonica.	2403,2778,2776
67) Vs. Melolontha vulgaris	3183,551,552
68) Vs. Lepidoderma. spp.	98
69) Vs. Heteronychus sanctae-helenae	3218,3219
70) Vs. Leptinotarsa decemlineata	3016,1872
71) Vs. Epitrix cucumeris	349
72) Vs. Diabrotica melanocephala and D. duodecempunctata	1262,1080,349,811
73) Vs. Phytonomus spp., Apion spp.	35
74) Vs. Hylobius radicis.	2813
75) Vs. Hypera meles.	2790
76) Vs. Tychius griseus.	2790
77) Vs. Sitona hispidula.	2790
78) Vs. Hylastinus obscurus.	1313
79) Vs. Cylas spp.	561
80) Vs. Pantomorus leucoloma.	248
81) Vs. Anthonomus grandis.	335,74,91
82) Vs. Anthonomus pomorum.	1104
83) Vs. Anthonomus pyri: Ineffective.	287
84) Vs. Anthonomus signatus: Inferior in effectiveness.	2143
85) Vs. Conotrachelus nenuphar: Taints fruit.	2914,2859
86) Vs. Musca domestica.	602
87) Vs. Musca domestica larvae.	2180,351,2179
88) Vs. Sarcoptes scabiei suis: Effective as 0.25 suspension sprays.	353
89) Vs. Sarcoptes scabiei and Chorioptis bovis of cattle: Effective as 0.6% sprays.	353
90) Vs. Demodex bovis: Effective as salves, but not as sprays.	353
91) Vs. Trombiculids, e.g. Eutrombicula alfreddugesi as dusts at 2 lbs/acre.	353
92) Vs. Dermanyssus gallinae: Taints eggs.	140
93) Vs. Boöphilus annulatus, as 0.5% sprays.	2841
94) Vs. Boöphilus decoloratus: Dips, and sprays 20 times as toxic as dusts.	3294
95) Vs. Dermatobia hominis.	1883
96) Vs. Amblyomma americana: As 0.5% suspensions.	2528
97) Vs. Dermacentor andersoni.	1271

14

BENZYL BENZOATE (Benzyl benzene carboxylate; Benzoic acid benzyl ester)



Molecular weight 212.24.

GENERAL

[Refs.: 2221,2288,2231,900,1810,1771,3033,2919,2852,3287,406]

An effective pediculicide and scabicide in topical application for sarcoptic, follicular, demodectic manges of man and animals. Useful and effective acaricide, as a clothing impregnant, against chiggers, *Trombicula* spp. Toxic for some plant Acarina, for example *Metatetranychus ulmi* active stages, but not ovicidal. Phenyl benzoate, a closely related compound, is toxic to *Tetranychus bimaculatus*.

PHYSICAL, CHEMICAL

Leaflet-like crystals, or an oily, colorless liquid of ethereal odor; m.p. 21°C; b.p. 323-324°C at 760 mmHg, 189-191°C at 16mmHg, 156°C at 4.5mmHg; d_4^{25} 1.118; n_D^{21} 1.568; insoluble, or sparingly so, in water; volatile in steam; soluble in alcohol, chloroform, ether, acetone, oils; insoluble in glycerol; sharp, burning taste.

Formulations: Numerous, for example:

a) May be used as such in solution at 20-25% concentration for *Pediculus humanus*, var. *corporis*, *capitis*, *Phthirius pubis*; for *Sarcoptes scabiei* at ca. 25% concentration. 2288
b) Compounded in an aromatized base as "B-B-S." 2288
c) As a stable emulsion: "Benlo" (benzylbenzoate 25% + benzylalcohol 2% + inert, non-alcoholic detergent base). 2288
d) "Benzamol-D", (benzyl benzoate 15% + DDT 1% + benzocaine 2%) 2288
e) "Colebenz" (per 100cc: Benzyl benzoate 33.3cc, cocoanut oil soap 6.5g, isopropyl alcohol q.s.) 2288
f) "Topocide," for use against head and body lice, crab lice, scabies mites, an aqueous emulsion: Per 100cc: 12.5g benzyl benzoate, 1g DDT, 2g benzocaine + polyoxalkalene derivatives of sorbitan monooleate. 2288
g) "Tyroscabe:" Benzyl benzoate, benzocaine, alcohol, tyrothricin. 2288
h) "Vanzoate lotion:" 25% benzyl benzoate in a quick drying base. 2288
i) "Zylate:" Benzyl benzoate 36%, isopropyl alcohol 52%, inert 12%. 2288

TOXICOLOGICAL

1) Toxicity for higher animals

Animal	Route	Dose	Dosage (cc/k)	
Mouse	or	LD_{50}	1.4	842
Rat	or	LD_{50}	1.7	842
Guinea Pig	or	LD_{50}	1.0	842
Rabbit	or	LD_{50}	1.8	842

a) Repeated use on human skin may sensitize. 2221

2) Toxicity for insects, Acarina:

Insect	Route	Dose	Dosage (cc/k)	Remarks	
Pediculus humanus corporis	Topical	LC_{50} (%)	22.0	Direct spray in oil (innocuous) to give 0.36mg/cm^2.	414
Cimex lectularius	Topical	LC_{50} (%)	75	" " " " (P31) " " " "	413

a) Much less toxic, in terms of concentration (%) to give 50% mortality, than several (7) organic thiocyanates, Lethane 60, Lethane 384, bisethyl xanthogen. However, the lower aliphatic thiocyanates are highly toxic and irritating to mammals. 414
b) Gives protection against chigger attachment; the impregnated clothing remained fully effective after two washings, partly effective after a 3rd washing. Related esters are effective vs. chiggers: 2919
(1) Benzoic acid, phenyl ester
(2) Benzoic acid, 3, 5-dimethyl phenyl ester
(3) 1,2,5,6-Tetrahydro-o-methyl benzoic acid
(4) 1,2,5,6-Tetrahydro-o-methylbenzyl ester
(5) Benzoic acid, α-methylbenzyl ester
(6) Benzoic acid, phenylethyl ester
(7) Benzoic acid, 2-chlorophenyl ester

c) More effective repellent for fleas, (as a clothing impregnant,) than dimethyl phthalate, q.v., Indalone® q.v., Rutgers 612, q.v. 2023

d) Excellent acavicide for trombiculid mites but not for plant feeding mites or insects. Highly useful vs. Eutrombicula spp. (vectors of scrub typhus) and chiggers. 3033 2919

e) As a 25% emulsion in one application can give up to 99% kills of Sarcoptes scabiei. 2852

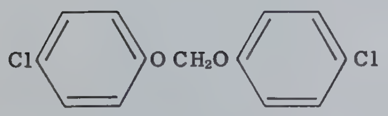
f) Inadequate at 5 lbs acre, to control Eutrombicula alfreddugesi (= Trombicula irritans) and Acariscus mansoni, in the field.

3) For screening test data see Ref. 1801.

15

BIS-(p-CHLOROPHENOXY)-METHANE

(di-4-Chlorophenoxy) methane; Oxythane; DCPM; Neotran®; K-1875.)



Molecular weight 269.1.

GENERAL

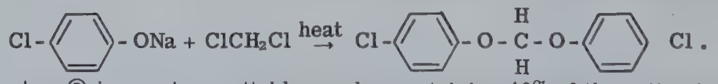
[Refs. 1697,1696,900,117,1801,1605,2821,2706]

An acaricide, particularly effective against all stages of Paratetranychus citri and Metatetranychus ulmi (= Paratetranychus pilosus); but of little insecticidal activity. Mites are quickly killed by Neotran® and it has some residual activity. Rather highly specific and not effective against many phytophagous Acarina. Persistent effect of 7 days in greenhouse. For screening tests with various insects and other arthropods consult Ref. 1801.

PHYSICAL, CHEMICAL

[Refs. 353,2231,2290,900]

Solid; colorless; almost odorless; m.p. 67°-68°C; not soluble in water; soluble in some organic solvents: Slightly soluble in alcohol, moderately soluble in benzene, carbon tetrachloride, readily soluble in ether, very soluble in acetone; insoluble in petroleum oils; stable in water and alkalis; decomposed in strongly acid solution and by boiling with dilute acid; compatible with the materials commonly employed in spraying; prepared as follows:



Formulations: Neotran® is a water-wettable powder containing 40% of the active ingredient, bis-(p-chlorophenoxy)-methane, and is used at the rate of 1.25-2.5 lbs/100 gallons of water.

TOXICOLOGICAL

1) Toxicity for higher animals:

a) Acute toxicity:

Animal	Route	Dose	Dosage (g/k)	Remarks	
Rat	or	LD$_{50}$	5.8 (5.0-6.0)		2933
Fish (Bluegill)	Medium	MLC(ca.)	0.1 ppm	Few deaths.	2026
Fish "	Medium	LC(ca.)	0.2 ppm	Toxic.	2026

b) Chronic toxicity:

(1) In prolonged feeding experiments rats showed no ill effects or growth retardation on diets containing 1000 ppm and 3000 ppm bis-(p-chlorophenoxy)-methane. Slight liver enlargement at the 3000 ppm dosage was noted. 2933

(2) On diets containing 10,000 ppm, rats showed irregularities of growth; death of 3 of 5 test animals occurred within 50 days. The dead animals showed fatty infiltration of the liver. 2933

(3) May be considered of low toxicity for man and mammals, both in acute and chronic intoxication. 2933

(a) Not irritating to nor absorbed by the skin. About $\frac{1}{10}$th as toxic as DDT. 2933

c) Hazard for wild life: None reported. 129

2) Phytotoxicity:
- a) The phytotoxic potential of bis-(p-chlorophenoxy)-methane is relatively low; it may, however, produce "russetting" of foliage in orchard trees (apple and pear varieties) and stunt the growth of some annual plants. 353 129
  - (1) 0.05% suspensions produced no injury (although some "russetting") in orchard trees; such succulent plants as beans and tomatoes may show foliage stunting. 2120 353
  - (2) 25% miscible formulations, at concentrations of 1:800 in water, have produced no foliage or flower injury on orchard trees or greenhouse plants. 353
    - (a) Higher concentrations do slight damage to peach and grape foliage and to Antirrhinum and Saint Paulia.
    - (b) 1:200 dilutions (of 25% miscible concentrate) may kill Boston and asparagus ferns.
  - (3) Not toxic to citrus plants even at concentrations of 4 lbs/100 gallons, sprayed at rate of 1500 gallons/acre, with temperatures 95°F or higher on each of the 10 days after treatment. 1697

3) Residues on treated vegetation.
- a) Residues on citrus: 0.2-14 ppm, depending on dosage and weathering. 129
  - (1) Orange fruits: Washing, according to commercial procedure, reduces residues of 8.1 ppm to 1.6 ppm.

4) Toxicity for Acarina, insects.
- a) Effective to a degree far beyond DDT for certain Acarina. 353
- b) Varies in degree of toxicity for diverse members of the Tetranychidae. 1697
  - (1) Closely related bis-(p-chlorophenoxy)-ethane is scarcely acaricidal at all. 2230
- c) As dosage per acre increases from 4 through 6,8,10,12 lbs, length of residual effectiveness and degree of control are enhanced. 1697
  - (1) High temperature conditions markedly shorten period of residual effectiveness.
- d) Vs. Paratetranychus:
  - (1) Paratetranychus citri, P. pilosus (=Metatetranychus ulmi) were effectively controlled by. 1697,1696,1605
    - (a) Effective as petroleum oil sprays with no difference between emulsions and wettable powders.
    - (b) 8 oz and 1 lb/100 gals as preventive spray control P. pilosus on apple trees, (with some "russetting.") 195
    - (c) Highly effective vs. P. pilosus and Septanychus schoeni mixed "populations" on apple trees. 1605
    - (d) As effective as parathion vs. P. pilosus. 2373,2374
- e) Vs. Septanychus:
  - (1) Ineffective against Septanychus sp(?) on cotton plants. 1640
- f) Vs. Tetranychus:
  - (1) Not effective for Tetranychus bimaculatus; 40 times less toxic for T. bimaculatus than for Paratetranychus citri. 2821 2230
  - (2) Effective against all stages of T. bimaculatus at 1 lbs/10 gallons. 117
  - (3) Parathion-resistant strain of T. telarius is not resistant to DCPM. 1116
  - (4) Less effective than parathion against T. pacificus. 2373,2374
  - (5) On citrus effective vs. T. sexmaculatus and T. lewisi only under special and restricted conditions (underleaf spraying, Spring application) because of the nature of the habitat of these forms. 1697
- g) Vs. others:
  - (1) Unsatisfactory control of Bryobia praetiosa at rates of 1 lb/100 gal. 2 applications. 191
  - (2) Inneffective against Aceria sheldoni. 1697,1699
  - (3) Ineffective against Phyllocoptruta oleivora. 1697
- h) Toxicity for various plant acarines:

Acarine	Route	Dose	Dosage	Remarks	
Tetranychus bimaculatus (adult)	Spray	LC_{50},g/100cc	0.62	Settling tower method; kill 2 days post treatment.	905
T. bimaculatus (larva)	Spray	LC_{50},g/100cc	0.215	" " " " "	905
T. bimaculatus (egg)	Spray	LC_{50},g/100cc	0.30	" " " " "	905
T. bimaculatus (adult)	Spray	LC_{50},g/100cc	5.0 +	Mites on leaf surface opposite the treated surface.	905
T. bimaculatus	Spray	LC_{50}, 24 hr (%)	>1.0		2230
Paratetranychus citri	Spray	LC_{50}, 24 hr, (%)	0.025	1% residues on orange still lethal after 2 months outdoor exposure.	2230

(1) Residual toxicity of bis-(p-chlorophenoxy)-methane as Neotran® 40% wettable powder for Tetranychus bimaculatus in greenhouse tests on Phaseolus coccineus: 117

Formulation	lbs/100 gal		% Mortality At Stated Period Between Spraying And Infestation of Plants With bimaculatus				
	Formulation	Active Ingred.	1 day	3 days	7 days	10 days	14 days
Neotran®	2.5	1.0	86.9	85.4	93.3	55.0	15.7

(2) Residual toxicity for Tetranychus bimaculatus; tested on Phaseolus coccineus, under greenhouse conditions at 1 lb/100 gal (2.5 lb of 40% wettable powder (Neotran®); more than 1600 mites examined in each test. 117

Days Between Spraying And Infestation	% Mortality After		
	7 days	14 days	21 days
1	78.6	86.9	84.7
2	66.9	76.5	66.7
3	68.5	85.4	81.2
4	75.0	88.1	73.1
5	73.9	78.0	61.7
6	81.9	83.4	48.6
7	77.1	93.3	46.7
10	63.6	55.0	43.6
14	11.3	15.7	23.8
CONTROL	5.0	7.7	–

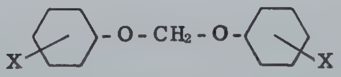
(a) Pronounced residual action; high mortality of all mite stages continuing for ca 1 week after spraying. The large numbers of eggs deposited by mites before death on deposits 4-5 days old were almost completely destroyed; on older deposits many eggs hatched and the young survived.

(3) Toxicity of bis-(p-chlorophenoxy)-methane compared with that of other substituted diphenoxy methanes: 2230

Compound	LC_{50} 24 hrs (%)	
	Paratetranychus citri	Tetranychus bimaculatus
Bis-(p-chlorophenoxy)-methane	0.025	>1.0
1,1-Bis-(p-chlorophenyl)-ethanol	0.1	0.035
Bis-(p-chlorophenyl)-methane	0.25	0.25
2-(p-Chlorophenyl)-1,1,1-trichloroethanol	0.2	0.4
p-(Chlorobenzyl)-p-chlorophenyl ether	0.13	–
Di-p-chlorophenyl ether	1.0 (= LC_{57})	–
p-Chlorophenyl-p-chlorobenzoate	1	–
Bis-(p-methylphenoxy)-methane	0.09	–
Bis-(p-bromophenoxy)-methane	0.1 (= LC_{96} 48 hr)	–
p-Chlorobenzyl-p-bromophenyl ether	0.9	–

(a) Order of acaricidal effectiveness in p,p′ substituents of bis-phenoxy-methane: $Cl < Br < CH_3 < NO_2 < CH_3O$.

(4) Toxicity of some bis (substituted-phenoxy)-methanes for Tetranychus bimaculatus and Epilachna varivestis: 1771



Ring Substitution (X)	Minimum LD_{100} 6 days (lbs/100 gallons) For		
	Tetranychus bimaculatus		Epilachna varivestis
	Adult	Egg	Larva
unsubstituted	3.0	>3.0	>3.0
2-chloro-	2.0	3.0	>1.0
4-chloro- (Neotran®)	1.0	0.25	0.5
2,4-dichloro-	>3.0	>1.0	>3.0
2,4,5-trichloro-	>3.0	>1.0	>3.0
2,4,6-trichloro-	>3.0	>3.0	>3.0
2,3,4,6-tetrachloro-	>3.0	>3.0	>3.0
pentachloro-	>3.0	>3.0	>3.0
4-bromo-	>1.0	3.0	0.5
4-nitro-	>2.0	–	>2.0
2-sec.-butyl-	3.0	3.0	0.5
X-tert.-octyl	>2.0	–	>2.0
2-allyl-	3.0	3.0	0.25
4-methoxy-	>3.0	>3.0	1.0
2,6-dimethoxy-	>3.0	>3.0	3.0
4-n-butoxy-	>1.0	>1.0	>1.0
2-chloro, 6 methyl	>2.0	>2.0	>3.0
2-chloro, 4-sec. butyl	>1.0	>1.0	>1.0
4-chloro, 2-methyl	>3.0	>3.0	>3.0
4-chloro, 2-sec. butyl	>1.0	>1.0	>1.0
4-chloro, 2-allyl	0.5	>1.0	0.5
6-chloro, 2-allyl	0.25	>1.0	0.25
2-allyl, 4-methyl	1.0	>1.0	>1.0
2-allyl, 4-methoxy	1.0	>1.0	0.12

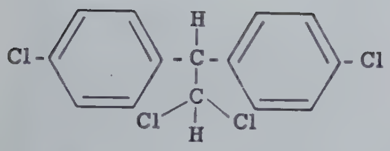
(5) Toxicity of bis-(p-chlorophenoxy)-methane for Metatetranychus ulmi (= Paratetranychus pilosus):

Concentration (% w/w)	% Mortality 24 hrs.	
	Summer Eggs	Adult ♀
0.1	57.8	87.8
0.1	—	91.8
0.025	28.9	56.2
0.025	—	53.1

16

2,2-BIS-(p-CHLOROPHENYL)-1,1-DICHLOROETHANE

(DDD; TDE; Dichlorodiphenyldichloroethane; Tetrachlorodiphenylethane; Rhothane®; Me 1700 [I.G. Farbenindustrie A.G.].)
(Analogue of DDT, having 1 less Cl atom on the chain)



Molecular weight 320.05

GENERAL

(Also consult DDT, DFDT, Methoxychlor, Perthane®)
[Refs. 1049,1933,2890,353,2231,2815,1059,757,129,2120,1801,3203,3150,2317,3162,647,1715]

A compound observed as an impurity of technical DDT. In practice, DDD has proved to be an insecticide of real value. Not as toxic as DDT for so wide a range of insects, but equal to DDT in toxicity for some insects, and superior in toxicity for certain others; for example, mosquito larvae, leaf rollers such as Argyrotaenia citrana and A. velutina, insects like the cornworm which have a well protected habitat, tomato and tobacco hornworms. For mammals, less toxic than DDT by $\frac{4}{5}$ to $\frac{9}{10}$, as a general approximation. $\frac{1}{4}$th - $\frac{1}{20}$th as toxic as DDT, orally, for rats; $\frac{1}{10}$th - $\frac{1}{20}$th as toxic as DDT for mice. Placed before the public under the same warning and precautionary labelling as is required for DDT.

PHYSICAL, CHEMICAL

Made by condensing monochlorobenzene and dichloroacetal (or dichloroacetaldehyde) in presence of sulfuric acid, or by chlorination, at 25-30°C (< 35°C), of ethanol, until the density of the lower layer is 1.29 at 20°C. The lower layer substance is then condensed, as described above, with monochlorobenzene.

Pure: A crystalline, colorless solid; the technical substance (setting point 86°C) is, like DDT, a mixture of isomers and related compounds with the o,p' -isomer predominant among the compounds other than p,p' -DDD. The o,p'-isomer is present to 7-8%, and has an m.p. of 76°C; p,p'-DDD has an m.p. of 109-110°C; b.p. 185-193°C; specific gravity 1.385; low vapor pressure; odorless; almost tasteless; not inflammable; more slowly dechlorinated than DDT in alkalis and alkaline solutions yielding, under such conditions, 2,2-bis-(p-chlorophenyl)-1-chloroethylene (m.p. 68°C). Less corrosive than DDT; insoluble in water; soluble in numerous organic solvents to different degrees; for example, in olive oil 10g/100cc at 37°C, acetone, methylethyl ketone, 10g/100cc, benzene 70g/100g, chlorobenzene 92g/100g, soluble in smaller quantity in many others; not decomposed by ultra-violet radiation under circumstances in which DDT is broken down. In presence of ferric chloride at 300°C, 2 moles of HCl are freed, yielding p,p'-dichlorotolane. The hydrolysis rate constant 10^5k, liters/sec/mole at 20°C = 567, at 37°C = 4035. Compatible with most standard insecticides and acaricides save lime-sulfur and Bordeaux mixture.

Formulated as: The technical product 100% (setting point 86°C); 50% wettable powders; 5-10% dusts; emulsifiable concentrates at 25% and 30% (solutions intended as household, livestock sprays). Dust usually applied at 10-15 lbs/acre; wettable powders as sprays of 1-3% concentration.

Being an analogue of DDT, with 1 less chlorine atom, DDD represents a product of one of several trends in the modification of DDT to give new analogues, in this case by subtraction, in others by addition, of chlorine atoms at the ethane location of the DDT molecule. Other alterations comprise change in position of chlorines on benzene rings, substitution of other halogens for chlorine, substitution of other than halogen radicals on the benzene rings.

Subtraction of chlorine from the 2-carbon of the ethane nucleus leads in general to decrease in insect toxicity in the following order: CCl_3 (DDT) > $CHCl_2$ (DDD) > CH_2Cl > CH_3. 2998

1) Comparative summary; hydrolysis, solubility, toxicity for lice, bed bugs, of DDD and related substances: 3288,418

Compound	LC_{50} (conc. %) Lice	LC_{50} (conc. %) Bed bugs	Hydrolysis (% After 240 min)	Solubility (w/v % at 18°C) Olive oil	Solubility (w/v % at 18°C) White oil
DDD	.9	1.20	33	10	1-2
p,p'-DDT	.3	.53	100	10	2-3
o,p-DDT (iso-DDT)	5.5	>20	13	25	10-14
Methoxychlor	.9	.55	10	8-10	1-2
Dimethyldiphenytrichloroethane	1.7	3.6	8	18-20	6-8
Diphenyltrichloroethane	7.5	>20	10	25-30	10-12
Dichlorodiphenylethane	8.5	>20	—	30	25
Dichlorodiphenyldichlorethylene	>20	>20	—	14-18	8-10

TOXICOLOGICAL

1) Acute toxicity, higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Man		EFD*	5000	* = Estimated Fatal Dose.	2221
Mouse	or	LD	2280		804
Rat	or	LD	3360		807
Rat	or	(?)MLD approx.	300	Neurotoxic symptoms; death in 1-12 days.	2890
Rat	or	LD_{50}	ca3400		1951
Rat	or	LD	2500		129
Rabbit	ct	LD_{50}	4000	As single acute inunction.	1952
Goldfish	Medium	LC_{50}	0.9 ppm	p,p'-DDT 0.06, o,p'-DDT 1.0, methoxychlor 0.06.	1187
Goldfish	Medium	LC_{100}	2.0	p,p'-DDT 0.25, o,p'-DDT 4.0, methoxychlor 0.25.	1187

2) Chronic toxicity, higher animals:
   a) Fed, at 100 ppm, to experimental animals in the diet for 2 year period: No gross effect. 1953
   b) Fed to experimental animals in diet, at up to 3750 ppm: No marked adverse effects; fat storage as high as 1290 mg/k. (Stored in fat and excreted in milk as with DDT) 1003, 129
   c) Rats, receiving DDD at 150 ppm for two years, stored 220 mg/k in the fat (similar dosage and treatment using DDT gave storage levels in fat of 2070 mg/k.) 186
   d) Dermal applications to rabbits, in daily inunctions of 200-400 mg/k were tolerated. 1952
   e) Among dogs, receiving in the diet 50-80 mg/k/day, 50% of the subjects survived after 21 months exposure. At autopsy: Liver damage namely: Atrophy, necrosis, cirrhosis, fatty degeneration. Marked atrophy of the adrenal cortex. 2361
   f) Among chickens, receiving 100 ppm in the diet, some died within 30 days showing subcutaneous and pericardial oedema. 3067
   g) Among cows, pigs, horses, sheep, goats, sprayed many times with 1.5% emulsions, no adverse symptoms appeared; calves, exposed to single sprayings of 8% emulsion, came to no harm. 407
   h) It has been generalized that the chronic toxicity of DDD is $\frac{1}{25}$th that of DDT; gross effects in animals appear at dietary levels of 2500 ppm. 1949

3) Effects on wildlife: Bobwhite Quail, receiving in diet for 6 weeks 250 ppm DDD, showed a mortality of 10%; similar treatment with DDT gave mortalities of 15-50%. 3223

4) Generalizations on toxicity for higher animals:
   a) For Rats: $\frac{1}{3}$rd as toxic by oral administration as DDT; $\frac{1}{4}$th as toxic as DDT by dermal administration; less toxic than DDT by inhalation except in kerosene spray. 1323
   b) Slightly irritating to the skin. 2890,3203
   c) Comparative toxicity DDD and DDT, for all animals tested: Average toxicity. 1949

Insecticide	Oral acute LD_{50}(mg/k)	Oral Chronic "LD_{50}" ppm	Cutaneous Danger Threshold (mg/k)	Pathology
DDD	2500	2500	2820	Adrenocortical.
DDT	250	100	2820	Hepatic, cerebellar.

   d) Less toxic for fish than DDT. 1187

5) Pharmacological, pharmacodynamical, physiological, etc.
   a) The action of DDD, save for its distinctly lesser toxicity, appears in general to be closely similar to that of DDT. Similar pathologies have been noted.
      (1) It has been reported that acute intoxication with DDD induces lethargy with an absence of convulsions. 2221

(2) Among the pathological changes storage of DDD in the adrenal cortex with atrophy and reduced adrenal function are notable and apparently almost unique to this chlorinated hydrocarbon insecticide. 2360,2361 2380,363 2381,1922

(3) Recent work reveals a marked decrease in adrenocortical responsiveness to adrenocorticotropic hormone in dogs receiving DDD as a 20% solution in corn oil at 100, 200 mg/k/day. 556

(a) The 17-hydroxycorticosteroid plasma levels fall from 20 to 0 μg/100cc.

(b) On discontinuance of DDD administration, normal responsiveness to ACTH gradually returned.

(c) Strikingly similar effects were noted in animals treated with DDD derivatives, namely: 2,2-bis-(p-ethylphenyl)-1,1-dichloroethane, (Perthane®) and 2-hydroxy-2,2-bis-(p-chlorophenyl)-1,1-dichloroethane (FW-152). Perthane® produced adrenocortical atrophy as did FW-152.

(4) Elimination of stored DDD from the fat of animals appears to take place more readily than elimination of stored DDT. 186

(5) In dogs and rats, DDD is excreted in feces, in small amount; none is found in the urine. The metabolic end-product is bis-(p-chlorophenyl) acetic acid, which shows up in greater amount than in DDT treated animals. 1003

(6) Hepatic pathology in dogs and pathological changes in chickens are noted above.

6) Phytotoxicity:

a) Not phytotoxic at normally applied insecticidal levels except possibly to certain Cucurbitaceae. 129,2120,353

7) Residue hazards:

a) Not to be used on forage crops intended for dairy animals or animals to be used for meat. 129,1425

b) Not to be applied to edible crops later than 30 days before harvest. 129

8) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti (larva)	Medium	LC$_{50}$	0.01 ppm	DDT, p,p' .01 ppm; o,p' 0.4 ppm; Methoxychlor 0.07 ppm.	1187
Aëdes aegypti (larva)	Medium	LC$_{100}$	0.05 ppm	DDT, p,p' .05 ppm; o,p' 5.0 ppm; Methoxychlor 0.2 ppm.	1187
Aëdes aegypti (larva)	Medium	LC$_{50}$	0.36 ppm		2168
Anopheles quadrimaculatus (larva)	Medium	LC$_{50}$	0.001 ppm	DDT 0.002 ppm.	767
Anopheles quadrimaculatus (adult) ♂	Topical	LD$_{50}$	0.041 μg/insect	Adults 4 days post-emergence.	2051
Anopheles quadrimaculatus (adult) ♀	Topical	LD$_{50}$	0.1 μg/insect	" " " " "	2051
Anopheles quadrimaculatus (adult) ♂	Topical	LD$_{90}$	0.098 μg/insect	" " " " "	2051
Anopheles quadrimaculatus (adult) ♀	Topical	LD$_{90}$	0.22 μg/insect	" " " " "	2051
Apis mellifera (adult)	or	LD$_{50}$	16.0 μg/bee	DDT 4.6 μg; BHC (90%γ) 0.15 μg; chlordane 1.2 μg.	910
Cimex lectularius	Contact Spray	LC$_{60}$	1.2%	Spray in white oil at 0.36 mg/cm^2.	418
Musca domestica	Topical (?)	LD$_{60}$	6.5 μg/g		2094
Musca domestica (DDT non-R)(adult)	Contact	LD$_{50}$ 24 hr	0.13 μg/fly	At 60°F; a "laboratory strain."	371
Musca domestica (DDT non-R)(adult)	Contact	LD$_{50}$	0.1 μg/g	DDT 0.02 μ/g; a "laboratory strain."	180
Musca domestica (Bellflower, DDT-R)	Contact	LD$_{50}$	60 μg/fly	Bellflower DDT resistant strain, adult.	371
Musca domestica (Bellflower, DDT-R)	Contact	LD$_{50}$	20 μg/g	DDT 10 μg/g; Bellflower DDT resistant strain, adult.	180
Musca domestica (Pollard, DDT-R)	Contact	LD$_{50}$	>100 μg/fly	Pollard DDT resistant strain, adult.	371
Pediculus humanus corporis	Contact Spray	LC$_{50}$	0.9%	Spray in white oil at 0.36 mg/cm^2.	418
Protoparce sexta (5th instar)	Topical	LD$_{50}$	2622 μg/larva	Large larva av. wgt. 5.4g (4.1-7.5g).	1306
Protoparce sexta (3rd, 4th instars)	Topical	LD$_{50}$	376 μg/larva	Medium larva av. wgt. 2.5g (1.2-4.0g).	1306
Protoparce sexta (2nd, 3rd instars)	Topical	LD$_{50}$	37 μg/larva	Small larva av. wgt. 0.9g (0.6-1.1g).	1306
Protoparce sexta (5th instar)	Topical	LD$_{90}$	9813 μg/larva	Large larva av. wgt. 5.4g (4.1-7.5g).	1306
Protoparce sexta (3rd, 4th instars)	Topical	LD$_{90}$	2620 μg/larva	Medium larva av. wgt. 2.5g (1.2-4.0g).	1306
Protoparce sexta (2nd, 3rd instars)	Topical	LD$_{90}$	367 μg/larva	Small larva av. wgt. 0.9g (0.6-1.1g).	1306
Protoparce sexta (5th instar)	or	LD$_{50}$	878 μg/larva	Large larva av. wgt. 5.4g (4.1-7.5g).	1306
Protoparce sexta (2nd, 3rd instars)	or	LD$_{50}$	22.5 μg/larva	Small larva av. wgt. 0.9g (0.6-1.1g).	1306
Protoparce sexta (5th instar)	or	LD$_{90}$	3192 μg/larva	Large larva av. wgt. 5.4g (4.1-7.5g).	1306
Protoparce sexta (2nd 3rd instars)	or	LD$_{90}$	58 μg/larva	Small larva av. wgt. 0.9g (0.6-1.1g).	1306
Sitophilus granarius (adult)	Contact	LC$_{50}$	4.53 x 10^{-6} moles/cc	Exposure 120 hr to deposits on paper from acetone solution.	2998
Sitophilus granarius (adult)	Contact	LC$_{95}$	169.1 x 10^{-6} moles/cc	Exposure 120 hr to deposits on paper from acetone solution.	2998
Chaoborus astictopus (larva)	Medium	CTC*	0.02 ppm	* = Concentration To Control; no fish hazard.	2019

9) Comparative toxicities for insects, DDD and other insecticides:

a) Contact insecticides for Pediculus humanus corporis and Cimex lectularius, as sprays in white oil. Insects treated by direct sprays at a deposit rate of 0.36 mg/cm^2: 636 414

Insecticide	LC$_{50}$ (%)	
	Pediculus	Cimex
DDD	0.9	1.2
DDT	0.3	0.5
Methoxychlor	0.9	0.5
DFDT	1.4	5.0
Lindane	0.02	0.05
p-Chlorophenyl chloromethyl sulfone	0.1	0.2
Lethane 384	1.5	—
Lauryl thiocyanate	5.0	—
Lethane 60	8.1	—

b) Toxicity of DDD, DDT, Methoxychlor for *Aëdes aegypti* larvae and the fish *Carassius auratus*: 1187

Insecticide	*A. aegypti*		*C. auratus*	
	LC_{50} (ppm)	LC_{100} (ppm)	LC_{50} (ppm)	LC_{100} (ppm)
DDD	0.01	0.05	0.9	2.0
p,p'-DDT	0.01	0.05	0.06	0.25
o,p'-DDT	0.40	5.0	1.0	4.0
Methoxychlor	0.07	0.2	0.06	0.25

c) Comparative toxicities for *Apis mellifera*: 910

(1) DDD may be considered one of the less toxic chlorinated hydrocarbons for the honeybee.

Insecticide	Oral LD_{50} (μg/bee)
DDD	16.0
DDT	4.6
BHC (90% γ-isomer)	0.15
Chlordane	1.2

d) DDD, and other insecticides, compared on the basis of speed of toxic action vs. *Macrosiphum pisi* on bean plants treated by the dusting tower method. Dust diluent: Talc: 520

Insecticide	Dust conc (%)	Temp (°F)	Time To Achieve	
			50% Kill (hrs: min)	98% Kill (hr: min)
DDD	5	72	2:34	4:35
DDT	5	72	0:57	1:45
Methoxychlor	10	75	2:1	5:34
Lindane	1	72	0:56	1:54
Toxaphene	5	72	13:20	19:1
Chlordane	5	72	9:24	18:8
Dieldrin	1	75	4:7	6:43
Aldrin	1	75	3:44	7:32
EPN	0.86	74	5:26	8:6
Parathion	1	70	1:8	1:43
Parathion	2	70	1:21	1:53
TEPP	0.18	74	0:20	0:56
Rotenone (5% other extractives 10%)	5	72	0:47	1:23
Nicotine	1	72	0:15	1:12
Nicotine	3	72	0:12	0:50
Talc	100	67-72	13:28	23:51

e) Comparative effectiveness of DDD and other compounds vs. *Periplaneta americana* and *Musca domestica*. Used as insecticide + urea-formaldehyde wall coatings at 50% insecticide (on dry weight of paint coating basis) vs. *Periplaneta* and 20% insecticide (on dry weight basis) vs. *Musca*: 267

Insecticide	*P. americana* Time For		*Musca* Time For 50% KD (minutes)		
	50% KD (hrs)	100% KD (hrs)	Initial	After Specified Interval	Interval (weeks)
DDD	>48	—	28	25	17
DDT	24	48	16	10	28
Lindane	1	1.5	13	16	6
Chlordane	15	18	60	41	7
Toxaphene	>48	—	48	35	12
Pyrethrum	—	—	18	2, 11, 23, 52	8, 14, 15, 17 days

f) Comparative toxicity DDD and other compounds. Topical application to *Anopheles quadrimaculatus*, 4 day old adults, in ethanol solution: 2051

Insecticide	LD_{50}(μg/insect)		LD_{90}(μg/insect)		Relative Effectiveness Compared To DDT			
					(at LD_{50})		(at LD_{90})	
	♂	♀	♂	♀	♂	♀	♂	♀
p,p'-DDD	0.041	0.1	0.098	0.22	0.49	0.66	0.46	0.59
p,p'-DDT	.020	.066	.045	.13	1.0	1.0	1.0	1.0
Methoxychlor (tech.)	.035	.1	.078	.22	0.57	0.66	0.58	0.59
Chlordane	.105	.24	.19	.46	0.19	0.28	0.24	0.28
Dieldrin	.009	.023	.022	.048	2.2	2.9	2.0	2.7
Lindane	.0085	.011	.032	.042	2.4	6.0	1.4	3.1
Toxaphene	.15	.29	.29	.5	0.13	0.23	0.16	0.26
Malathion	.0087	.0095	.019	.022	2.3	7.0	2.4	5.9
Allethrin	.0029	.008	.013	.041	6.9	8.3	3.5	3.2

g) Comparative toxicity DDD and other compounds for Protoparce sexta larvae. Topical and oral administration; small larvae = 0.9(.6-1.1)g av. wgt. 2, 3rd instars, medium = 2.5(1.2-4)g av. wgt, 3, 4th instars, large = 5.4(4.1-7.5)g av. wgt. 5th instar: 1306

Insecticide	Size	Topical (µg/larva)		Oral (µg/larva)	
		LD_{50}	LD_{90}	LD_{50}	LD_{90}
DDD	Large	2622	9813	878	3,192
"	Medium	376	2620	—	—
"	Small	37	367	22.5	58
DDT	Large	≫4000	—	4416	28,040
"	Medium	2334	9887	—	—
"	Small	366	1342	158	1,125
Endrin	Large	42	219	9.9	49
"	Medium	2.9	6.3	—	—
"	Small	0.51	6.3	0.11	0.85
Parathion	Large	52	183	15.7	54
"	Medium	9.9	64	—	—
"	Small	2.8	12.3	—	—
Isodrin	Large	87	490	15.3	138
"	Medium	7.6	29	—	—
"	Small	3	56	1.1	3.1
Toxaphene	Large	1363	5778	143	6,025
"	Medium	32	138	—	—
"	Small	30	112	—	—
Malathion	Large	481	1276	355	1,621
"	Medium	61	553	—	—
"	Small	23.6	92	—	—
Dieldrin	Large	482	2559	—	—
Aldrin	Large	487	1359	—	—
Lindane	Large	206	1235	209	398
Heptachlor	Large	1058	4005	—	—

h) Comparative control obtained in 2 successive years, using DDD and other compounds vs. cabbage caterpillars, Pieris rapae (predominant in 1946) Trichoplusia ni (predominant in 1947): 796

Insecticide	Conc. Dust (%)	% Control Obtained In	
		1946	1947
DDD	3	—	87.0
DDT	1	—	81.9
"	2	87.5	87.5
"	3	88.9	87.6
Methoxychlor	3	—	60.9
Chlordane	3	—	72.6
Toxaphene	3	—	80.8
Lindane	0.38	84.2	—
"	1	—	62.7
Rotenone	0.75	85.8	35.5
Ryania	30	83.1	—
"	40	—	46.0
Sabadilla seed	10	84.5	—
Pyrethrum	20	78.6	—
Lead arsenate	20	77.6	—
Calcium arsenate	20	—	0
Zinc fluoarsenate	20	26	—
2-Mercapto-6-nitrobenzothiazole	10	3.8	0
Least Significant Difference (5% level)		11.4	14.0
" " " (1% ")		16.4	18.6

i) Toxicity of DDD and other compounds. Topical application to Heliothis zea and Heliothis virescens, 6th instar larvae of 250-450 mg weight, in methylethylketone solution applied to the abdominal dorsum: 1124

Toxicant	LD_{50} (µg/g) For	
	Heliothis zea	Heliothis virescens
DDD	3000	17,000
Toxaphene	2000	18,000
DDT	3000	6,500
Endrin	17	180
Malathion	130	160
Dipterex®	30	60
Bayer 17147	40	54
Shell OS-2046	4.8	4.8

10) Pharmacological, pharmacodynamical, physiological; insects:

a) There seems no reason to believe that the mode of entrance and action of DDD in the insect body differs 353
markedly from that of DDT, in spite of various nuances and specificities connected with the insects 2231
treated and the methods used. The theories of toxic action proposed for DDT apply.

(1) Replacement by H of a single Cl of the trichloromethyl group of DDT to give DDD, brings about, in 415,2040
general, a decline in insect toxicity by $\frac{3}{4}$ths to $\frac{1}{2}$. Nevertheless, in some cases, for example vs. 767,2975
Anopheles quadrimaculatus, Protoparce sexta, Argyrotaenia velutinana, and A. citrana DDD is 418,2317
somewhat more potent than DDT. Progressive unchlorination of the ethane group leads to further 2337,2551
decline in insect toxicity until (with the completely unchlorinated ethane) toxicity to insects is all 2998,1187
but lost, although acaricidal activity is high. The fumigant properties of DDD are reported to be 353,2230
inferior to those of DDT.

(2) As with DDT and methoxychlor, insect mortality with DDD is greater at lower than at higher temperatures; 1561
there is a negative temperature coefficient of action. This has been demonstrated for Musca 1305
domestica which, exposed to residual DDD deposits at 70°F and 90°F, showed higher mortalities at the 1559
lower temperature. The same effect has been demonstrated for other insects using various routes of
application.

(3) Application of DDD (dusts), as in the case of DDT, methoxychlor, and other DDT derivatives to 2041
Oryzaephilus surinamensis in toxic concentrations brings on sharp increase in O_2 consumption. The
effect does not follow sub-lethal dosages. Total O_2 uptake of control and treated insects did not significantly
differ under starvation conditions.

(4) At concentrations of 10^{-3} M, DDD (and other chlorinated hydrocarbons) was found in vitro to produce 2305
total inhibition of ♂ Periplaneta americana coxal muscle cytochrome-c-oxidase; at 10^{-5} M a slight
transient stimulation was noted. The inhibition with DDD was rapid (in the case of DDT the onset of
inhibition was slow).

(5) The site of action of DDD (as of DDT) appears to be on the neuromuscular system. DDD, applied to the 1901
leg of Periplaneta americana, produced trains of repetitive discharge, observable on the oscillograph
beginning at 1 hour after application (more rapidly than with DDT, and at a lower voltage than with
either DDT or methoxychlor).

(6) The characteristic action (on the nerve axon of Periplaneta americana) of DDT was imitated closely by 3278
DDD (and other analogues). This comprised: Multiplication of the nerve impulse into a prolonged 1226
burst of impulses which resulted in tetanic contraction of the muscle served by the nerve axon. Duration
of the impulse train was found to be directly proportional to concentration. In severe intoxication,
spontaneous trains of impulses occurred periodically without external stimulus.

b) Metabolism of DDD by insects:

(1) By Argyrotaenia velutinana (for which DDD is more toxic than DDT, although both pass into the cuticle 2975
at similar rates) DDD is less readily dehydrochlorinated than DDT and may be recovered from the
insect tissues.

(2) By Epilachna varivestis (for which DDD is non-effective) rapid metabolism of DDD occurs, with pro- 2975
duction of 2,2-bis-(p-chlorophenyl)-chloroethylene and further degradation to unknown compounds.

c) Resistance ("acquired"), of insects to DDD:

(1) In certain strains of DDT-R Musca (products of selection in presence of the insecticide) a parallel 180
resistance to DDD is noted. For example the Bellflower strain, derived from the Ellenville wild strain, 371
has a contact LD_{50} for DDT of 20μg/g (as contrasted with 0.02μg/g in the laboratory strain of origin); 2231
for DDD the LD_{50} (contact) of the Bellflower strain is 20μg/g (for the DDT-nonR laboratory strain of
origin 0.1μg/g). The same phenomenon of parallel DDT and DDD resistance was shown by the Pollard
strain (DDT-R).

11) DDD in the economic control of insects; field experiences:

a) For the residual treatment of walls to control mosquitoes the order of effectiveness of DDD and others: 2466
DDT > methoxychlor > methyl-DDT > DDD > DFDT.

b) Vs. Simulium spp: As effective as DDT; superior to chlordane, toxaphene, lindane, BHC. 1192

c) Gnats were controlled by 0.014 ppm of DDD emulsion without harmful effects upon fish and "fish food 2014
organisms."

d) Chaoborus, and chironimid larvae were controlled in 35 days by application of 0.013 ppm DDD. (These 2014
organisms form 10-20% of certain fish diets)

e) As direct sprays for cattle, effective in control of Siphona irritans. 788,2183

f) Vs. Melophagus ovinus: Although inferior to BHC, toxaphene, chlordane and methoxychlor, 0.2% suspen- 959
sions (as dips or sprays for lambs) gave 4 month long control.

g) For tortricids (Argyrotaenia spp.): Superior to DDT in control. 353

h) Vs. Halticus bracteatus: DDD yielded good results. 3279

i) Vs. Erythroneura comes and Dykraneura sp: DDD aerosols gave control and proved less hazardous but 353
less persistent in effect than DDT.

j) Vs. Protoparce sexta and P. quinquemaculata: 10% dusts are more effective than cryolite. 821

k) Vs. Estigmene acraea: Ineffective. 91

l) Vs. Cirphis, Prodenia, Laphygma (armyworms): Equal in effect compared to DDT in control when used 1572
as a dust.

m) Vs. Heliothis armigera: As a 0.25% suspension spray proved superior to DDT and Ryania in control. 1875

n) Vs. Argyrotaenia citrana: 0.2% solutions gave 99% control. Superior to other chlorinated hydrocarbons, 2704
cryolite and parathion.

o) Vs. Grapholitha molesta: As a 0.1% spray, only slightly less effective than DDT. 560

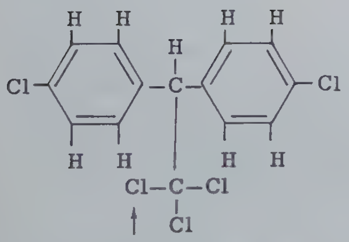
p) Vs. *Carpocapsa pomonella*: Unsatisfactory as a control agent. 2379
q) Vs. *Diaphania nitidalis*: 5% dusts gave control. 69
r) Vs. *Gnorimoschema operculella*: Single sprays at 0.1% were equal to 0.1% DDT in control. 1571
s) Vs. *Liriomyza orbona*: 5% dusts gave 80% control. Inferior to chlordane which yielded 99% control. 1913

For screening test data consult Ref. 1801.

17

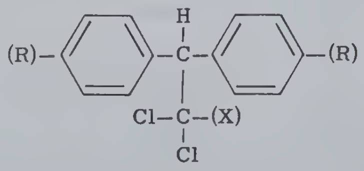
2,2-BIS-(p-CHLOROPHENYL)-1,1,1-TRICHLOROETHANE

(DDT; Dichlorodiphenyltrichloroethane; 1,1,1-Trichloro-2,2-bis-(p-chlorophenyl)-ethane; Trichloro-bis-(4-chlorophenyl)-ethane; α,α-Bis-(p-chlorophenyl)-β,β,β-trichloroethane; Chlorophenothane (=pharmaceutical grade of DDT); Dicophane (=official designation in Great Britain); Gesarol; Neocid; p, p′ -DDT; etc., etc.)



DDT Molecular weight 354.5

CHIEF INSECTICIDAL ANALOGUES (q.v.)



Where R = Cl, X = Cl-DDT
" " = CH_3O, = Cl-Methoxychlor
" " = Br, = Cl-Colorado 9
" " = F, = Cl-DFDT
" " = Cl, = H -DDD or TDE

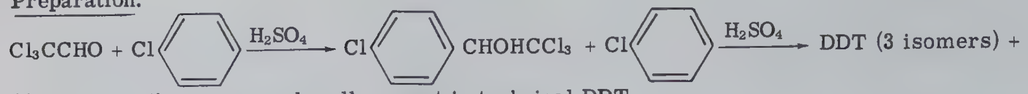
GENERAL [Refs. 353,2231,2815,1059,757,2226,129,2120,1933,2317,3287,3155,3199,2184,1221,89,1935,2660,426,2661,619,620,1352,1801,1564,799,2874,2072,2010,1622,1155,3070,3388,1535,1401,3115,2948,761,3342,929]

A chlorinated hydrocarbon, synthesized and described chemically in 1874. The insecticidal properties of DDT remained unknown until 1939. The advent of DDT as an insecticide was a virtual revolution in the concepts of insect control and enormously widened the possibilities. The range of activity shown by DDT against insects, was exceptional in the number of genera and species susceptible to its action within the economic limits of use. DDT showed, moreover, unprecedented properties as a residual toxicant. Everything in the nature of DDT gave promise of applications hitherto unknown. The interest excited by DDT stimulated studies of insect pharmacology and insecticide pharmacodynamics which greatly enlarged exact knowledge in these fields. These studies opened the way for design of synthetics with particularly desirable properties in insect control and which balanced high insecticidal potency with relatively low hazard for man, domestic animals, and wild life. Increasing evidence of biotypes of many insects resistant to DDT does little to diminish the lustre of this insecticide and its close analogues. This phenomenon has added more to practical knowledge than it detracts from practical success in control of harmful insects. If nothing else, it serves as a warning against ultimate triumphs taken for granted, absurd expectations, and unbalanced enthusiasm.

DDT has been the subject of a vast outpouring of scientific papers and field reports. Several treatises and monographs specifically devoted to it are readily available. The present treatment can only cover the most salient and illustrative parts of this extensive material. However, its very abundance places within reach of any interested person ample and readily available information on all aspects of this exceptional insecticide.

PHYSICAL, CHEMICAL [Refs.: 1049,353,2231,3199,1345,2719,171,2120,129,2221,73,1721,1871,1059,643,645, 1020,2087,252,1019,1297,3253,163,540,973,2229]

1) Preparation:



11 or more other compounds, all present in technical DDT.

Technical DDT; Approximate Composition (Samples vary widely)

Compound	(%)	Toxicity* PH LC_{50}%	Toxicity* CL LC_{50} %	Toxicity* AQ LC_{50} ppm	Toxicity* DM LC_{50} relative
2,2-Bis-(p-chlorophenyl)-1,1,1-trichloroethane (p,p'-DDT)	63-77	0.3	0.53	0.002	1
2-o-Chlorophenyl-2-p-chlorophenyl-1,1,1-trichloroethane (o,p'-DDT)	8-21	5.5	>14	0.012	145
2,2-Bis-(o-chlorophenyl)-1,1,1-trichloroethane (o,o'-DDT)	0.1-1	5.0-7.5	—	—	—
2,2-Bis-(p-chlorophenyl)-1,1-dichloroethane (p,p'-DDD)	0.3-4	0.9	1.2	0.0025	17
2-o-Chlorophenyl-2-p-chlorophenyl-1,1-dichloroethane (o,p'-DDD)	0.04	—	—	—	—
1-o-Chlorophenyethyl-2-trichloro-p-chlorobenzene sulfonate	0.1-1.9	6.5	>10	10	25
2-Trichloro-1-p-chlorophenylethanol	0.2	—	—	—	—
Bis-(p-chlorophenyl) sulfone	0.03-0.6	—	—	1.0	> 50
α-Chloro-α-p-chlorophenyl acetamide	0.01	—	—	—	—
α-Chloro-α-o-chlorophenyl acetamide	0.01	—	—	—	—
Chlorobenzene	0.3	—	—	—	—
p-Dichlorobenzene	0.1	—	—	—	—
2-(p-Chlorophenyl)-1,1,1,2-tetrachloroethane	trace	—	—	—	—
Sodium p-chlorobenzene sulfonate	0.02	—	—	—	—
Ammonium p-chlorobenzene sulfonate	0.01	—	—	—	—
Inorganic constituents	0.01-0.1	—	—	—	—
Unidentified, etc.	5.1-10.6	—	—	—	—

*PH = Pediculus humanus corporis, CL = Cimex lectularius, AQ = Anopheles quadrimaculatus, DM = Drosophila melanogaster.

Technical DDT: A white to cream-colored waxy solid or amorphous powder; m.p. indefinite; minimum setting point 89°C; solubility very similar to pure p,p'-isomer (see below); contains 9.5%-11% hydrolyzable chlorine, 1% alcohol insoluble and volatile material. There are three important isomers which make up DDT, viz., p,p'-, o,p'-, o,o'-isomers. The p,p'-isomer is the potent insecticide.

Pure DDT (p,p'-isomer): White solid in colorless, needle-like, or tabular crystals; m.p. 108.5°-109°C; decomposition at ca. 110°C; b.p. 185°C at 1 mmHg; $d_{4°}^{25°}$ 1.556 (also given as 1.6, 1.52); v.p. 1.5×10^{-7} mmHg at 20°C; tasteless; virtually insoluble in water (to 0.1 ppm at 18°C); moderately to readily soluble in most organic solvents (see below); stable and inert in neutral media; in alkaline media hydrolyzes, freeing HCl; $10^5 k$ (l/sec/M) at 20.1°C = 2480, at 30.4°C = 7110 with sodium hydroxide + ethanol as the hydrolyzing medium; pure DDT is relatively stable toward heat, decomposing rapidly at >195°C; tech. DDT, less stable due to impurities, decomposes at ca. 100°C; iron, anhydrous ferric- and aluminum chlorides, and ferric oxide catalyze the decomposition; most solvents antagonize the heat decomposition (save chloro- and nitro- benzenes which accelerate it). Fe^{+++}-philic agents, e.g. picolinic acid, salicylaminoguanidine, at 2% inhibit catalytic breakdown; residual deposits, fully exposed to the environmental ultra-violet radiation, decompose slowly into substances non-toxic for insects; v.p. at 45.7°C 6.9×10^{-5}, at 61.5°C 2.6×10^{-4}, at 71.3°C 7.6×10^{-4}, at 90°-100°C 3.3×10^{-3}.

Formulations: Dusts, wettable powders, emulsions in water, solutions in various solvents, aerosols, smokes, gas by vaporization, aerosols with pyrethrins, numerous agricultural sprays and dusts of various DDT concentrations and formulations. 1061

Solubility Of Purified DDT In Various Solvents

Solvent	Grams DDT per 100 cc	Grams DDT per 100g	Solvent	Grams DDT per 100cc	Grams DDT per 100g
Acetone	58	74	Dimethyl phthalate	34	29
Acetonyl acetone	38	39	1,4-Dioxane	92	89
Acetophenone	67	65	Dipropylene glycol	5	5
Amyl acetate	39	44	Ethanol (95%)	2	2
Anisole	70	70	Ethyl benzoate	57	54
Benzene	78	89	Ethylene dichloride	59	47
Benzylacetate	45	43	Ethyl ether	28	39
Benzyl alcohol	12	11	Fuel oil #1	8-11	10-14
Benzyl benzoate	42	38	Fuel oil #2	7-10	8-12
Benzyl ether	41	39	Furfuryl alcohol	7	6
Indalone	38	35	Gasoline	10	13

Solubility Of Purified DDT In Various Solvents

Solvent	Grams DDT per		Solvent	Grams DDT per	
	100cc	100g		100cc	100g
Butyl stearate	8	9	Isopropanol	3	4
Carbon tetrachloride	45	28	Kerosene	8-10	10-12
Castor oil	7	7	Linseed oil (raw)	11	12
p-Chloroacetophenone	39	33	Methyl salicylate	40	34
Chlorobenzene	74	67	Morpholine	75	75
1-Chloronaphthalene	55	46	Nitroethane	27	26
Cinnamaldehyde	25	22	Oleic acid	8	9
Cottonseed oil	11	12	Peanut oil	11	12
Cresylic acid	17	17	Phenyl ether	42	39
Cumene	37	43	Pine oil	10-16	11-17
Cyclohexane	15	19	Propionic acid	16	>16
Cyclohexanol	10	11	Propylene glycol	< 1	—
Cyclohexanone	116	122	Stoddard Solvent	9	12
Cyclohexylbenzoate	46	44	Tetrahydronaphthalene	61	63
p-Cymene	29	34	Tributyl phosphate	50	51
Dibutyl phthalate	33	32	Triethanolamine	< 1	—
o-Dichlorobenzene	59	45	o-Xylene	57	66
Diethylene glycol monobutylether	34	36	Xylene (commercial)	53	61

Solubility Of DDT Compared To That Of DFDT, The Fluorine Analogue

Solvent	g/100cc		Solvent	g/100cc	
	p,p'-DDT	p,p'-DFDT		p,p'-DDT	p,p'-DFDT
Mineral Seal oil	3.9	83	Carbon tetrachloride	45	650
Kerosene (white)	8-10	140	Xylene	53	670
Dibutyl phthalate	33	260	o-Dichlorobenzene	59	700
Polymethyl naphthalenes	57	460	Cyclohexanone	116	850

TOXICOLOGICAL

1) Toxicity for higher animals: [Refs.: 2350,3199,89,851,1221,1949,3217,2221,246,353]

a) Toxic for higher animals (as well as for many lower organisms, other than insects). With appropriate understanding and precautions hazard is low. The toxicity is less than that of such substances as sodium fluoride, Paris green and nicotine long used successfully in house and field.

(1) Acute LD_{50}, oral, (average of animals tested) = 250 mg/k, chronic "MLD" = 100ppm, cutaneous danger level ≑ 2820 mg/k.

(2) For comparison (in same order as above:) DDD 2500, 2500, 2820; Methoxychlor 7000, 5000, 2820; Lindane 125, 400, 50; Chlordane 500, 250, 1880; Toxaphene 60, 780 (cutaneous; Nicotine 10, 60, 50).

(3) Oral dose to produce illness in some human subjects: 10 mg/k; convulsive dose 16 mg/k or >; known dosage consumed sans fatality in one case = 285 mg/k; even small doses may induce vomiting which makes accurate determination of actual dosage difficult.

(4) Estimated oral LD, Man: 500 mg/k, with death in 2-24 hours; LD in kerosene solution = ca 150 mg/k.

(5) Least daily repeated dose to produce illness: Unknown. On basis of animal tests, 2.5-5.0 mg/k/day is the estimate for mild intoxication. Dogs tolerate 10 mg/k/day for years sans effect, but man is more sensitive; a 10 mg/k dose makes some subjects ill in single dosage; 0.5 mg/k/day induces no overt effect and 50 ppm in the daily diet is necessary to yield this amount.

(6) Actual average concentration of DDT in prepared meals: Ca 0.25 ppm (0.0026 mg/k/day.)

b) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Frog	sc	LD	50		1563
Frog	sc	LD_{50}	34.64	Death within 48 hrs; in dorsal lymph sac.	3129
Frog; Tadpoles	Environment	LC	1 lb/acre	Ponds, average depth 5".	604
Tadpole	Medium	LC	0.1 ppm (laboratory tests), 0.25 ppm (field tests)		1885
Mouse	or	LD_{50}	ca180		3360
Mouse	or	LD_{50}	150-250		246
Mouse	or	LD_{50}	200	In olive oil.	3203
Mouse	or	LD_{50}	400	In olive oil; in corn oil.	839,818
Rat	or	LD_{50}	420	In liquid paraffin.	3360
Rat	or	LD_{50}	800		450
Rat	or	LD_{50}	ca200	In liquid paraffin.	2497
Rat	or	LD_{50}	200	In corn oil; in peanut oil.	839,2497
Rat	or	LD_{50}	150	In olive oil.	2895
Rat	ct	LD_{50}	3000	In ether and other solvents, e.g. kerosene.	450
Rat	sc	LD_{50}	1500	In liquid paraffin + tragacanth.	450
Rat	ip	LD	100-200		1563
Rat	iv	LD_{50}	40-50	As an emulsion.	1519
Rat	iv	LD_{50}	60	Emulsion in lecithin.	2497

b) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Guinea Pig	or	LD_{50}	400	In liquid paraffin; in corn oil.	839,450
Guinea Pig	or	LD_{40}	282-355		3360
Guinea Pig	ct	LD_{50}	1000	In ether, kerosene, etc.	450
Guinea Pig	sc	LD_{50}	900	In liquid paraffin + tragacanth.	450
Rabbit	or	LD_{50}	300-500		246
Rabbit	or	LD_{50}	300	In olive oil; in liquid paraffin.	450,2895
Rabbit	or	LD_{50}	400	In liquid paraffin.	3360
Rabbit	or	LD_{50}	250	In liquid paraffin.	450
Rabbit	ct	LD_{50}	300	In ether, kerosene, etc.	450
Rabbit	ct	LD_{50}	2820		1949
Rabbit	sc	LD_{50}	>3200	In corn oil.	1519
Rabbit	sc	LD_{50}	250	In paraffin oil + tragacanth.	450
Rabbit	ip	LD_{50}	2100	In olive oil.	1519
Rabbit	iv	LD_{100}	50	Emulsion in lecithin.	2497
Rabbit	iv	LD	40-45	In olive oil.	2497
Cat	or	LD_{50}	400-600	In peanut oil.	2497
Cat	or	LD_{50}	400-500	As emulsion.	2497
Cat	iv	LD_{100}	40-50	Emulsion in lecithin.	2497
Cat	iv	LD	40-75	As emulsion.	2497
Dog	iv	LD	60-75	As emulsion.	2497
Dog	iv	LD_{50}	ca 50	Emulsion in lecithin	2497
Monkey	or	LD_{50}	> 200		246
Monkey	iv	LD_{50}	60	Emulsion in lecithin.	2497
Calf	or	MTD*	250	*Minimum Toxic Single Dose.	2567
Cattle	or	MTD*	500	" " " " "	2567
Sheep	or	MTD*	500	" " " " "	2567
Horse	or	MTD*	> 234	" " " " "	2567
Horse	or	LD_{50}	> 300		246
Bob-white Quail	or	LD	ca300	In crystalline form.	557
Bob-white Quail	or	LD	60-85	In oil solution.	557
Duck (Mallard, Pintail)	or	Toxic	1000	No deaths; toxic symptoms.	557
Starling	or	Toxic	600	No deaths; liver lesions.	557
Rabbit (Cottontail)	or	MLD	ca2500		557
Deer (white-footed) Mouse	or	LD_{50}	ca1500	Death within 24 hrs; symptoms in all.	557
Deer (white-footed) Mouse	or	LD_{100}	ca2000	" " 3-49 hrs.	557
Chicken	or	LD_{50}	>1300		246
Goldfish	Medium	LC_{50}	0.1 ppm		2396
Goldfish	Medium	LC_{100}	0.2 ppm		1937
Bluegill (fingerling)	Medium	LC_{100}	0.15 ppm		1937
Bass (fingerling)	Medium	LC_{100}	0.05 ppm		1937
Gambusia	Medium	LC_{50}	0.01 ppm		2396
Salmo gairdnerii (1.5")	Medium	LC	0.15 ppm	(.25 lb/acre) 54.2°F, suspension, 18 l aquaria.	2362
Salmo trutta (1.5")	Medium	LC	0.15 ppm	(.25 lb/acre) " " " "	2362
Salvelinus fontinalis (1.6")	Medium	LC	0.15 ppm	(.25 lb/acre) " " " "	2362
Tilapia kafuensis (young)	Medium	Toxic C	0.04 ppm	Dirt ponds; > sensitive in aquaria.	2505
Micropterus dolomieu (young)	Medium	LC	1 lb/acre	Aerial spray; adults not affected.	1566
Catasomus commersonii (young)	Medium	LC	1 lb/acre	" " " " "	1566
Hypentelium nigricans (young)	Medium	LC	1 lb/acre	" " " " "	1566
Fish	Medium	LC	0.01-1.0 ppm		1937,1885
Fish	Medium	LC	0.25 ppm		1507,2717
Fish	Medium	LC	0.4 lb/acre; .05-1.6 ppm.	As a dust.	3050,1885,1937,3232
Fish	Medium	Toxic C	0.004-5.0 ppm	Kerosene, oil, acetone sols.	1192,1184,2429,928,44,3237
Fish	Medium	Toxic C	0.05 lb/acre		3050
Fish	Medium	MTL 10 days*	0.15 ppm	*Mean Tolerance Limit, 10 days exp.	828
Crayfish (Crustacea)	Medium	LC	0.25-1.0 ppm		1885
Crab, Crayfish, Amphipods (Crustacea)	Medium	LC	1 lb/acre	As a dust on ponds.	604
Daphnia (Crustacea)	Medium	LC_{100}	0.1 ppm	Laboratory tests.	1885
Daphnia (")	Medium	IT*	0.001-0.1 ppm	*Immobilization Threshold.	67

(1) Minimum Toxic Concentration (%) as a single total surface spray or dip of DDT: 2567

Baby calves = >8%
Cattle = >8%
Sheep = >8%
Pigs = >8%
Horses = >8%

Oral toxicity of solid DDT for several domestic animals; ST = by stomach tube, GC = in gelatin capsules, IF = in feed: 3067

Animal	Weight (k)	Dosage (g/k)	Remarks
Goat ♀	38.5	1.5 ST	Mild tremors → recovery.
" "	49.8	1.5 ST	Mild tremors → recovery.
" " (young)	22.2	2.2 ST	Moderate tremors → recovery.
" "	42.6	2.8 ST	Severe tremors → prostration (52 hrs) → killed.
" ♂ (young)	17.2	2.9 ST	Light tremors → recovery.
" ♀ (")	24.9	3.3 ST	Moderate-severe tremors → recovery.
" ♂	57.9	5.5 ST	Severe tremors → convulsions → prostration (13 day) → killed
" ♂	38.5	6.5 ST	Severe tremors → death on 16th day.
Horse (gelding)	562	0.26 IF	No symptoms or signs of toxicity.
Chicken (W. Leghorn)	2.25	0.44 GC	No symptoms, signs; some laid eggs following treatment.
" (" ")	2.16	.46 GC	
" (" ")	2.6	.39 GC	
" (" ")	2.4	.42 GC	
" (Barred Rock)	1.44	.35 GC	No symptoms, signs; all gained weight following treatment.
" (" ")	1.5	.49 GC	
" (" ")	1.44	.35 GC	

(2) Toxicity of DDT in "jar tests" for Carassius auratus (Goldfish), exposed so that 5 fish shared 2.5 liters of tap water: 1184

Alcohol Solution				Surface Application In Oil				As Dusts			
DDT	% Kill After			DDT lbs/acre	DDT Dilution	% Kill After		DDT lbs/acre	Dilution	% Kill After	
	1 day	2 days	6 days			3 days	6 days			3 days	6 days
.05 ppm	0	0	0	0.42	.4 ppm	30	60	0.1	.1 ppm	0	33
.1 ppm	0	0	40	0.85	.8 ppm	40	60	.2	.2 ppm	17	33
.133 ppm	20	30	80	1.7	1.6 ppm	60	80	.5	.4 ppm	17	33
.2 ppm	60	100	—	CONTROL	—	0	0	1.0	1 ppm	17	33
.4 ppm	90	100	—	—	—	—	—	2.0	2 ppm	33	100
.5 ppm	90	100	—	—	—	—	—	2.0	2 ppm	17	66
1.0 ppm	90	100	—	—	—	—	—	CONTROL	—	0	0
2.0 ppm	100	—	—	—	—	—	—	—	—	—	—
4.0 ppm	100	—	—	—	—	—	—	—	—	—	—
10.0 ppm	100	—	—	—	—	—	—	—	—	—	—
CONTROL	0	0	0	—	—	—	—	—	—	—	—

c) Repeated doses, sub-acute, sub-chronic, chronic, other toxicity:

(1) Dog: [Refs.: 2348,1322,3199,1953]
or 100 mg/k/day, as 4 doses/day in capsules, for 7 wks gave no effect.
or 10 mg/k/day, in corn oil, tolerated sans effect for 3 years.
or 80 mg/k/day, dry form, gave no effect.
or 50, 80 mg/k/day, in corn oil, produced death in several months.
inh 12.44 mg/l (10% dust) 3 hrs/day, 4 wks, gave no toxic effects.
insufflation 100 mg/k (10% dust)/day gave toxic signs (in $\frac{1}{3}$) after 18 days; tremor; liver, kidney damage.
ct 1cc (3% sol)/day, 3 wks, then 3xs/day, 4 wks gave $\frac{3}{4}$ kill; severe CNS depression; no pathology.

(2) Rat: [Refs.: 1955,3360,2050,3069,1322,1931,1323,450]
or 50 ppm (diet) → no overt effects; 100 ppm → slight chronic poisoning; 400-800 ppm → CNS effects, tremors.
or 5-10 ppm gave micropathology in liver, moderate at 50 ppm; marked at 400 ppm.
or 250 ppm (diet), 52 wks exposure, gave no effect, according to some.
or 1000 ppm (diet) yielded unmistakable toxic effects; young: Dead in 14-18 days, symptoms in 6-13 days.
or 2000 ppm gave 50% kill within 9 days; 1200-1800 ppm fatal in < 1 week; 300-600 ppm: Mortality ratio = to controls.
or 800-12,000 ppm yielded definite toxic signs, some deaths; 600 ppm tolerated for 14 wks, 100% fatal after 52 wks. 100-800 ppm for up to 2 yrs produced chronic toxicity in all.
inh 4-10 exposures at 1000 ppm in air (initial), 2hrs/day brought death. Aerosols at 6.2, 12.4, 54.4 mg/l, initial DDT concentration, 45 minute exposures gave no effect.
ct 200 mg/k/day (10% kerosene sol.) proved fatal in 14 wks; weaker solutions also were fatal over longer exposure periods. 15, 50 mg (pure, dry DDT) or as 5% dust, 2 hrs/day exposure yielded no toxic effects.

(3) Mouse: [Refs.: 3360,2348,2349,450]
or (in diet) 125, 250, 500 ppm brought death in 1-6 days.

inh Aerosols at 6.22 mg DDT/l were tolerated in presence of 6% sesame oil; toxic effect in presence of 9.5% sesame oil; >6.22 mg/l always toxic (excitability, nervousness, tremor, convulsions). 0.183 mg/l, 45 minute exposures 3xs/day gave definite toxic signs not noted in single exposure tests.

ct 0.1cc (3% sol.) fatal to most; 0.025, 0.012cc gave definite toxic signs.

(4) Rabbit; Guinea Pig: [Refs.: 2348,2349,3360,2895,840,450,3199]

or Rabbit, 40mg/k in olive oil proved toxic in repeated doses.

or Guinea pig, 1000 ppm (diet), 52 wks exposure proved definitely toxic.

inh Rabbit, Guinea pig, 1000 ppm at 2 hrs/day: Fatal after 8-9, 9-10 exposures.

inh Guinea Pig, Aerosols 6.2, 12.4, 54.4 mg DDT/l (initial), tolerated sans toxic signs.

ct Rabbit, 3.9, 6.0, 9.4 cc/k 30% DDT in dimethyl phthalate on shaved skin gave toxic signs, no deaths; 100 mg/k (as 10% sol.) in kerosene produced death in 6 days of repeated application.

ct Guinea pig, 200 mg/k/day in kerosene proved fatal in 14 days.

ct Rabbit, 1, 2, 3 cc/k 30% sol. in dimethyl phthalate, proved fatal, in daily inunction, to all; some deaths at 0.5 cc/k; toxic signs, no deaths at 0.25 cc/k 13 wks exposure.

(5) Chicken: Refs.: [3199,2571]

or, 500 ppm (diet) yielded death of young birds in 4-16 days; at 1000 ppm brought death in 3-10 days. Not to be used as a spray or dip on birds.

(6) Farm Animals: [Refs.: 2420,2571]

or, Cows, horses, sheep, 100 mg/k/day (1 week), then 150 mg/k/day (2nd week) followed by 200 mg/k/day (3rd week) yielded CNS symptoms in most cows; no toxic signs in sheep, horses.

or Cows, sheep, 4-5 months on pea vine silage treated at 1 lb DDT/ton fresh wgt showed no toxic signs, but 15 ppm DDT was present in milk.

topical (spray, dip) 8% DDT, 1 application tolerated by all; 10 applications 2% DDT at 2 wk intervals deemed safe; 36 applications 0.5% DDT at 2 wk intervals tolerated by cattle; cattle, horses, sheep, goats, tolerated 8 applications at 4 day intervals of 1.5% DDT.

(7) Comparative oral toxicity, farm animals, DDT, and other compounds: 3277

Insecticide	Animal	Wgt (lbs)	g/k	Remarks
DDT	Sheep	85	2	Extreme nervousness, muscle spasms 24 hrs-5 days; normal 9th day.
DDT	Sheep	97	1	Muscle tremor; failure of coordination.
DDT	Sheep	93	0.5	Slight nervous symptoms for 24 hrs.
DDT	Steer	540	0.5	Nervousness, twitching, lack of coordination; normal 6th day.
BHC (10% γ)	Sheep	86	2	Extreme symptoms in 6 hrs; spasms, blindness; normal 5th day.
BHC (")	Sheep	124	1	Slight nervous symptoms in 24 hrs; soon normal.
BHC (")	Sheep	90	0.75	" " " " " "
BHC (")	Steer	710	0.125	No effect.
Chlordane	Sheep	78	2	Severe respiratory and nerve symptoms in 16 hrs; death at 48 hrs.
Chlordane	Sheep	123	1	"
Chlordane	Sheep	103	0.5	Incoordination, nervousness, blindness; normal on 5-6 day.
Chlordane	Steer	820	0.05	No effect.
Methoxychlor	Sheep	115	1	Normal.
Methoxychlor	Sheep	83	2	Normal.
Methoxychlor	Steer	540	0.5	No effect.

d) Hazard to man and animals in water supply: 247,476

(1) Aerial spraying of DDT at 1 lb/acre, 10.4 mg/ft^2 gave 0.36 ppm in waters 1 ft deep, 0.0735 ppm in waters of average 5 ft depth. Overall average of 0.1 ppm is assumed.

(2) No harm to city water supplies from applications at 0.1-2 lb/acre (0.01-0.2 ppm) since ordinary treatment of such waters removes most of DDT present at original concentrations of 0.1-10 ppm.

(3) Reservoir water, treated at 0.01 ppm, yielded far less than the minimum toxic concentration for man in consumed water. Normal use vs. mosquito larvae is innocuous to warm-blooded animals.

(4) Mice, receiving as sole water supply 10 ppm DDT-containing water for 75 days, showed no deleterious effect; at 50 ppm for 58 days showed no effect.

e) Toxicity, hazard for wild life:

(1) DDT is toxic to fish. Damage is proportional to dose and particularly serious in shallow bodies of water. Toxicity varies with species and age. Stable emulsions tend to be more toxic than oil solutions and dusts; water dispersible powders tend to be the least toxic. 3020,3022 1567,3050 247

(2) Sprayed aerially at 0.1 lb/acre, 5 times as much DDT is recoverable at water surfaces than when aerosol is used. Maximum recovered at surface, using thermal aerosol at 0.1 lb/acre was 0.012 lb/acre. 3050 1758

(3) Aerial spraying of forests (e.g. vs. *Porthetria dispar*) at 1 lb/acre gave 70%-80% loss of fish food organisms. 1565 1564

(4) Field experiences; DDT and Wildlife:

I) Aerial spraying on 2 watersheds, DDT in oil formulation (1 lb DDT, 1 pt xylene, 7 pts kerosene) at 1 gallon/acre: Stream flowing at 17.7 ft^3/sec, 8000 gals/minute; 2 lakes (1 = 15 acres, 16 ft deep 1565 at dam, 1 = 60 acres, av. depth 25 ft.:) Heavy deaths of fish in stream and lakes from direct and wind-borne spray, particularly in areas of double spraying (overlap). Great numbers of fish dead after heavy feeding on DDT-killed and disabled insects drifting downstream in great numbers. Most fish were susceptible, e.g., *Notemigonus crysoleucas*, *Catasomus commersonnii*, *Ameiurus nebulosus*, *Esox niger*, *Lepomis gibbosus*. Mortality of fish began generally during 1st day and continued for ca. 1 month. Virtual elimination of fish from shallow ponds. Stream waters toxic to test fish (with typical symptoms of DDT poisoning.) Native fishes taken in treated area showed typical DDT toxic symptoms. Stream waters, 18 days post-treatment, were lethal to 4 inch goldfish in 8-12 hours. Effects were cumulative as spray washed down stream. 70-80% kills of bottom insects were followed by heavy deaths among fishes (e.g. trout) feeding thereon. On a stream, 6 miles long, av. width 20-25 ft., sprayed over its whole watershed at 1 lb/acre DDT and sampled at mouth: Heavy fish mortality 1 day post treatment, continuing for 3 weeks.

II) Summary of Special Scientific Report on DDT and wildlife: 2362

1) At 1.1 lb/acre on forest land brought no change in bird census.

2) At 3 lbs/acre on dense forest: Amphibians killed, bird numbers unchanged, mammals unharmed on 64 acre test area.

3) At 5 lbs/acre on forest land yielded 15% decline in bird census.

4) At 2 lbs/acre on salt marsh yielded complete kill of 4 crab species; no effect on 2 snail and 1 mussel species.

5) Pine forest, 4xs sprayed at weekly intervals with 1% DDT in oil, ground deposit average 0.2 lbs/acre, 0.58 lb/acre maximum, showed great reduction of insects; birds unaffected. Nestling birds, fed spruce budworms, killed by forest spraying of DDT at 1 lb/acre, at 25%, 50% of body wgt in insects/day showed no DDT poisoning. Laboratory killed insects (DDT sprays), given to nestling birds which fed to repletion for 2 days, and to 25% of body wgt on 3rd day, caused death of 7/27 directly by DDT poisoning and contributed to deaths of 8 others.

6) Aerial application at 1 lb/acre, DDT wettable powder, average deposit 0.39 lb/acre gave little effect on many kinds of minnows; various native fishes of the current year's hatch were affected with heaviest mortality noted in 3-4 days and continuing until 7th day. 10% of warm-water fishes exposed above, within or below, treated area were killed.

7) DDT in oil at 1-2 lbs/acre, followed in 1 month by 0.26 lb/acre gave moderate harm to fish on 2500 acres so treated for mosquito control.

8) Cottontail rabbits, exposed on pastures treated at 5 and 7.5 lbs/acre DDT in oil, all died within 9 days with typical symptoms; controls unharmed.

9) In aquarium studies, DDT oil sprays and suspensions at 0.25, 0.5 lb/acre, gave 100% kills of bluegills. Trout, treated at 0.25 lb/acre in aquaria with mud bottoms, showed 0.37% mortality, without mud, 84%-100% mortality. Rainbow trout proved particularly sensitive.

10) DDT suspension, at 1 lb/acre over raceways of hard spring water with brook and rainbow trout, bass, golden shiners, showed 3-4 inch long trout not affected.

11) In "*Daphnia* ponds" containing fingerlings, exposure to DDT suspensions at 1 lb/acre brought serious effects to black crappie, small-mouth bass, bluegill; large-mouth bass, rainbow trout, golden shiner were relatively little affected. Two inch bluegills exposed unfed showed 25% mortality; fed showed 12% mortality. Rainbow trout, 3-3.75 inches, exposed unfed showed 45% mortality; fed showed 5% mortality.

12) Advanced fry of large- and small-mouthed bass in dirt bottom ponds with ample natural food, exposed to 0.37, 1.0 lb DDT suspension/acre and 0.5 lb/acre oil spray in 12 day tests: With DDT suspension: No survival; with DDT in oil: No survival in 2, 12% survival in 1 pond. Fingerling black crappie, bluegill, brown bullhead sprayed in various ponds at 0.5 lb/acre DDT suspension and 0.37, 0.5, 1.0 lb/acre oil formulations showed 61% or greater kill in oil treated ponds; 8-78% kill in suspension treated ponds. At 1 lb DDT/acre oil solutions and suspensions were equal in toxicity to fish.

13) Deaths among adult birds, mammals, begin when DDT concentrations reach 3 lbs/acre application rate; amphibians are also affected. To avoid fish, crab, and crayfish injury spray at 0.2 lb (or <)/acre and at < 2 lbs/acre to avoid harm to birds, mammals, amphibians in forest areas. In emulsion form even smaller amounts are desirable. Direct application should not be made to streams, lakes, or coastal bays. Early insects should be dealt with before major spring bird migrations; late pests, if possible, should be dealt with after the bird nesting season.

14) Oysters: No effect on oysters at 5 lbs/acre. Dipping of oyster spat collecting surfaces almost 2037
completely prevents barnacle fouling. Sprayed at 200 mg/ft^2 on spat collecting surfaces, inter- 3243
fered neither with oyster or barnacle settling.

III) For experiments, in detail, on the effect of feeding to various fishes, (e.g. *Micropterus dolomieu*, *M. salmoides*, *Lepomis macrochirus*, *Pomoxis nigro-maculatus*) diverse insects treated with different DDT formulations consult Reference 1567.

1) *Micropterus dolomieu*, receiving DDT wettable powder in gelatin capsules at 50, 100, 200 mg/k, all showed DDT toxic symptoms in several hours and all were dead in 24-29 hours.

IV) Other data, toxicity of DDT formulations for fish: 1566

1) *Micropterus dolomieu*, *M. salmoides* (ca 1 inch fry) in dirt bottom ponds, average midnight temperature, 75.7°F:

25% wettable powder at 0.041, 0.065, 0.1 ppm (0.37, 0.5, 1 lb/acre) gave 100% mortality.
DDT in oil (1 lb/gal) at 0.085, 0.09 ppm (ca 0.5 lb/acre) gave 100% mortality.
" " " " at 0.07 ppm (ca 0.5 lb/acre) gave 87-88.5% mortality.

(Controls in all cases showed survival of from 81.5 to 95%.)

2) Formulation: DDT 1 lb, 3180 cc PD-544-B (naphthenic solvent, + fuel oil to make 1 gallon:
Micropterus dolomieu (av. 1.1 inches) 0.09 ppm (0.5 lb/acre) showed 85% mortality in 48 hrs; 100% mortality within 5 days. (Controls: 100% survival).
M. dolomieu (av. 1.25 inches) 0.04 ppm (0.25 lb/acre) at 75°F showed 100% mortality in 48 hrs in concrete ponds; (Controls: 97% survival).
Lepomis macrochirus (av 1.0 inch) 0.04 ppm (0.25 lb/acre) at 72.9°F showed 70% mortality (3 days), 80-90% mortality (4 days); (Controls: 100% survival).
Notemigonus chrysoleucas (adults, fry): 0.065 ppm gave 100% mortality of fry, survival of adults.
" " (fry): 0.025 ppm gave 100% mortality in 48 hrs at 72°F (av.)
" " ("): 0.014 ppm gave no effect, 9 day exposure, 72°F (av.)

3) Formulation: 50% wettable powder:
Lepomis macrochirus (1.0 inch): 0.09 ppm gave 70.5% mortality in dirt bottom ponds.
" " " : 0.085 ppm gave 66% " " "
" " " : 0.07 ppm gave 16% " " "
(Controls 79.5-89.0% survival)
Pomoxis nigro-maculatus (0.17 g av.): 0.085 ppm gave 77.5% mortality in dirt bottom ponds.
" " " " : 0.09 ppm gave 65.5% " " "
" " " " : 0.07 ppm gave 14.5% " " "
(Controls 82-98% survival)
Ameiurus nebulosus (1.2 inch av.): 0.07 ppm gave 10.5% " " "
" " " : 0.085 ppm gave 49% " " "
" " " : 0.09 ppm gave 7.5% " " "
(Controls 89.5-95% survival)

4) Formulation: DDT 1 lb, xylene 2 pints + No. 2 fuel oil to make 1 gallon:
Lepomis macrochirus (1.0 inch av.): 0.04 ppm gave 87% mortality in dirt-bottom ponds.
" " " : 0.065 ppm gave 76.5% " " "
" " " : 0.1 ppm gave 70% " " "
(Control 79.5%-89% survival)
Pomoxis nigro-maculatus (0. 17 g av.): 0.04 ppm gave 69% " " "
" " " : 0.065 ppm gave 92.5% mortality in dirt-bottom ponds.
" " " : 0.1 ppm gave 77% " " "
(Control 82%-92.5% survival)
Ameiurus nebulosus (1.2 inch av.): 0.04 ppm yielded 61% mortality in dirt-bottom ponds.
" " " : 0.065 ppm yielded 87.5% " " "
" " " : 0.1 ppm yielded 80.5% " " "
(Control 89.5-95.0% survival)
Micropterus dolomieu (2.7 inches av.): 0.14 ppm gave 46%, 54% mortality in dirt ponds.
Micropterus salmoides (adult, 10-15 in): 0.14 ppm (2 sprayings, 7 day interval) gave 0 mortality.
" " (4.9 inches av.): 0.14-0.17 ppm gave little effect.
Lepomis macrochirus (3.6 inches av.): 0.14-0.17 ppm gave 50-60% mortality in dirt ponds.
" " (3.8 "): 0.13-0.14 ppm gave 8%, 24% " "
" " (adult, 6-7 in.): 0.14 ppm (2 sprayings, 7 day interval) gave 0 mortality.

5) Other experiments: Formulations: A = 50% wettable powder (commercial), B = 1 lb DDT, 2 pints xylene, No. 2 fuel oil to make 1 gallon;
Tests in 20 liter aquaria at 61.8°F av. temp., DDT at 0.28 ppm (0.5 lb/acre)

Formulation A; B	*Lepomis macrochirus*	100% mortality	Heaviest mortality 2-3 days after application.
	Trout (rainbow)	100% "	
	Trout (brook)	100% "	

Tests in raceways of flowing water with A at 1 lb/acre, maximum possible concentration = 0.258 ppm: Negligible mortality among *Notemigonus chrysoleucas*, *Micropterus dolomieu*, brook and rainbow trout.

6) Differences in mortality of several fish exposed to 2 different commercial preparations of 50% water wettable powder at 0.18 ppm (1 lb DDT/acre):

Preparation	% Survival, Duplicate Tests In Daphnia Ponds			
	M. dolomieu (3.2")	*M. salmoides* (2.6")	*L. macrochirus* (2.0")	*N. chrysoleucas* (3.3")
I	46; 86	22; 40	24; 30	18; 48
II	98; 98	72; 82	32; 42	96; 98
Control	100; 100	82; 96	56; 78	74; 82
I	26; 30 (3.1")	98; 100 (2.8")	18; 24 (2.1")	96; 98 (3.1")
II	22; 22	88; 94	4; 14	100; 100
Control	94; 96	100; 100	98; 100	100; 100

	Rainbow Trout	Black Crappie
I	92; 98	0; 16
II	82; 94	2; 4
Control	100; 100	84; 90

Black crappie mortality heavy immediately after application; *M. dolomieu*, *L. macrochirus* mortality heavy at 2-4 days post-application.

7) Mortality in dirt-bottom ponds of several fish exposed to DDT water wettable powders, commercial, at 50% DDT (A), 90% DDT (B):

Preparation	DDT (ppm)	% Survival M. dolomieu		M. salmoides		L. macrochirus		N. chrysoleucas	
A	0.09	94	77 (av)	95	76.3 (av)	98	72 (av)	50	68.7 av
A	0.14	88		86		98		92	
A	0.17	49		48		20		64	
B	0.10	100	78.7 (av)	82	69 (av)	100	84 (av)	88	82.7
B	0.11	77		64		86		72	
B	0.13	65		61		66		88	
Control (av. of 3 replicates)		85.3		86.7		100		86.7	

V) DDT and wild birds; game birds

1) For data on acute toxicity consult the stated references: 557,679
2) DDT at 1 lb/acre is reported to have no apparent effect on numbers of wild birds; at 5 lbs/acre marked reduction in wild bird numbers is reported. 1599,2673 1223,2278
3) After 5 applications of DDT, at 2 lbs/acre, a 26% decrease in breeding wild birds is reported. 2672
4) Prolonged exposure to DDT affects breeding potential of birds even in absence of immediate effects, sub-lethal amounts accumulate in tissues and organs. 1931
5) Failure of breeding in adult ♂ quail, with death when tissue accumulated DDT was > 30-35μg/g has been noted. 2080 782,557
6) Effect of DDT in the diet of quail, pheasants; experiments in continuous feeding of DDT-containing rations: 780

Bird	No.	DDT %	 ppm	DDT Consumed/day (mg/k)	Total Consumed (mg/k)	Mortality (%)	Survival Time (days)
Quail (adult)	40	0.025	250	25	1100	100	45
" "	10	0.020	200	13.8	2125	10	154
" (young)*	80	0.01	100	10.5	1260	30	
" Control (adult)	96	—	—	—	—	4.1	154 (test pd)
" " (young)*	200	—	—	—	—	28.5	120 (" ")
Pheasant (adult)	16	0.025	250	11.5	208	100	18
" (young)*	20	0.005	50	4.6	475	35	
" Control (adult)	108	—	—	—	—	3.6	100 (test pd)
" " (young)*	200	—	—	—	—	31.5	100 (" ")

*Birds 1 day old at experiment's beginning; test duration 120 days unless otherwise shown.

Effect On Reproduction of quail:

DDT %	 ppm	Eggs/Hen/day	Fertility (%)	Hatchability (%)	% Chicks Surviving (DDT-free Diet) At 1 wk	 3 wks	 12 wks
0.02	200	0.35	93.6	66.8	43.8	36.2	19.8
0	0	0.53	88.6 *	82.3 **	90.0	87.5	78.3

*Difference not statistically significant. **Difference significant P = 0.08.

DDT (ppm) During Winter	 Reproduction	% Mortality	Eggs/Hen (Av.)	% Fertile	Hatch (%)	Chicks Surviving (%) At 2 wks	 6 wks
100	0	0	61	87.5	75.7	86.2	64.3
100	100	25	65	66.9	75.3	67.7	7.1
0	200	25	55	92.8	80.0	32.3	12.9
Control		6.25	52	89.0	83.9	88.9	83.3
Pheasants							
0	50	0	31	81.4	58.6	100	85
50	50	0	18	77.5	80.6	100	93.3
0	100	0	19	86.2	52.0	100	82.4
Control		0	48	86.6	57.4	94.8	89.7

a) At 0.01% (100 ppm) in the diet, experiments 1-10 wks in duration little effect of any kind on the growth or survival of young quail could be detected.

Effect of DDT on quail and pheasants when fed during growth:

Bird	DDT (ppm)	Duration Test (days)	Mortality (%)	DDT Consumed/day (mg/k)	DDT Consumed (Total) (mg/k)
Quail	150	15	53.3	7.2	10.8
Quail	100	120	30	10.5	1260

a) At 0.01% (100 ppm) in the diet, experiments 1-10 wks in duration little effect of any kind on the growth or survival of young quail could be detected.

Effect of DDT on quail and pheasants when fed during growth:

Bird	DDT (ppm)	Duration Test (days)	Mortality (%)	DDT Consumed/day (mg/k)	DDT Consumed (Total) (mg/k)
Quail (control)	0	120	24	–	–
Pheasant	100	51	100	21.2	1130
"	50	103	37	4.6	475
" (control)	0	103	28	–	–
		Fed during winter maintenance			
Quail*	100	162	20.2	7.3	1180
" (control)	0	162	8.7	–	–
Pheasant*	50	120	42.9	2.5	300
" (control)	0	120	12.5	–	–

*Birds which had received similar levels of DDT in diet during growth period.

(7) Other observations, wild birds, mammals: 557

(a) Quail (Bob-white), feeding tests using 5 week old birds; test period 63 days:
At 0.005% in the diet: Some deaths attributable to DDT.
At 0.025% in the diet: 50% mortality of tested birds.
At 0.05-0.4% in the diet: Death of all tested birds; at 0.05% of 10 birds 2 were dead on 7th day, 8 on 14th day, all on 28th day;
At 0.1%, 0.2% all dead on 7th day. At 0.4% all dead by end of 1st day of exposure.

(b) Ducks (Mallard; Pintail): Toxic reactions noted at dietary levels of DDT > 0.025%.

(c) Cottontail Rabbits:
At 0.2% in diet for > 3 days: Toxic symptoms in some.
At 0.4% 3 of 4 animals dead by 21st day of exposure via the diet after severe tremors; focal necrosis in liver, kidneys.

(d) Meadow Mouse:
At 0.2% in the diet: Tremors in all; death of 2 out of 5 subjects within 28 days.
At 0.4% in the diet: 5 out of 5 subjects dead by 21st day.
At < 0.2% in diet: All subjects survived the 31 day test period.

(e) Deer (White-footed) Mouse: Toxic signs only on diets containing > 0.1% DDT; at 0.2 and 0.4% in diet tremors developed on 3rd day of exposure which disappeared on 5th day and did not return during 30 day test period.

2) Pharmacological, pharmacodynamic, physiological, etc., higher animals:

a) Mode of entry: Gastrointestinal, pulmonary (in case of aerosols, dusts, mists), via skin (if in solution or emulsion). Gastrointestinal absorption is enhanced by presence of fats and oils of whatever source. 89,2348 840,2895

b) Effect on skin: No primary irritation; irritation due to diluents and solvents is possible. Sensitization is confirmed by some, denied by others. Non-carcinogenic in tests on mice of strain "C." 89,840 872,221

c) Distribution in body after entry: Wide distribution in tissues and organs. Rat, 5 hrs after 500 mg/k, oral: μg/100g in liver 600; spleen 600; heart 600; brain 500; adrenals 4000; kidney 500; lung 700; blood 2000. Goat, after 3 (500 mg/k) doses in oil, 4 days after last dose: mg/100g in fat (omentum) 1121; lymph nodes (mesenteric) 307; adrenal 288; heart 267; thymus 163; testis 41; liver 35; kidney 21.5; spleen 18; spinal cord 17; brain 15.5; lung 14. 1935 2939 3069
(1) Passes the placental barrier (goat), to affect the foetus, if present in sufficient concentration.

d) Accumulation in body: Accumulates in body fat and in such lipid rich materials as egg yolk, milk, etc. If exposure is continuous, tends to reach in the body fat a steady plateau balanced by a slow, steady elimination. 3361 3363 3358
(1) ♀ rat stores more than ♂. 1879
(2) Storage noted (dog) at 1 ppm in the diet. 1930
(3) Stored in human fat in subjects exposed to DDT. 1406
(4) Fat levels may be high in animals without any toxic signs. 380
(5) 50% of DDT content of body fat is reported to be as DDE, 2,2-bis-(p-chlorophenyl)-1,1-dichloroethylene. 1929,89 576,2462

e) Excretion: Largely via kidney, but not as DDT per se; in part as the metabolite di-(p-chlorophenyl)-acetic acid (DDA), excreted also after administration of DDE, 2,2-bis-(p-chlorophenyl)-1,1-dichloroethylene, which may thus be a metabolic intermediate. 3292,2399, 1927,2347 1736,2896,3361 3068,234,1929
(1) Rabbits, rats, man: Bulk of excretion, after single dose, in first 5-6 days continuing in < degree for 10 days or more; 1.8-5.1% of total dose is excreted, with 10% recoverable, in urine, feces. In repeated exposure, only a small amount is steadily excreted as DDA; the bulk is stored, to be gradually lost as DDA after end of exposure. 2896,1927 3068,1929 234,3361 2939,89
(2) Present in bile, in milk, in eggs.

f) Site of principal pharmacodynamic action: Principal action is on the central nervous system, and is 2497,2207
manifested as: Apprehension, excitement, hyperreflexia, locomotor disturbances, muscle tremors, 244,851
and finally, tonic and clonic convulsions. 89

(1) Definite effect upon the cerebellum; electroencephalogram similar to that in human 'Grand Mal', is 640
noted in cats and monkeys. Degenerative changes are demonstrable in the cerebellar tissue structure. 1455
2520

(2) In Frog: Action antagonized by curare. Section of nerve abolished tremors peripheral to site of section. 3129
Section of posterior spinal root afferents did not abolish motor effect. Section of spinal cord caudad to 845
bulb did not prevent hyperreflexia, tremors. Application directly to brain and cord induced tremors
and motor effects. Thus the effect was not on muscle tissue proper. Facilitated synaptic transmission.

(3) Effect on mammalian nerve is veratrine-like. 955

g) Other effects:

(1) Kidney: No evidence of deleterious effect on organ function. 2348,2207,1736

(2) Liver: Some distinct effects noted viz., mobilization of hepatic glycogen (rat): depression of 1934,1678
lactic acid formation by liver slices of DDT treated subjects (rat); alterations in oxygen uptake, 1931,2207
both up and down, are reported; increased lipid content of liver. No change reported in liver 2647,2739
excretion of total or inorganic sulfate, creatine, or creatinine. 2348

(3) Biochemical: Increase in total oxygen uptake has been reported. No increase in uptake of oxygen by 2647
isolated muscle (frog, sartorius) or muscle breis (rat). 1736

(4) Effect on enzyme systems: No effect on aldolase, adenosine triphosphatase, choline oxidase, succinic 1736
oxidase, pyruvic oxidase, lactic or malic dehydrogenase, triose phosphate dehydrogenase, creatine 2001
phosphokinase or phosphorylating systems at 5×10^{-4} M concentration. Increase reported in chicken
plasma choline esterase activity with repeated daily subcutaneous dosage.

h) Pathological: [Refs.: 89,1931,1017,3360,2359,2348,2349,450,2896,1995,1994,1930,452,221,3199,851,1221]

(1) The principal pathological findings in experimental DDT poisonings (primarily in rats, rabbits,) are liver changes. These changes may be generalized as: Centrolobular hypertrophy, flight of cytoplasmic granules to the cell margin, fatty infiltration and degenerative changes. Hepatic cell necrosis is associated, in all animals, only with elevated DDT dosage. A hepatic "tumorogenic" tendency has been ascribed to DDT on the basis of several studies.

(2) Changes in the kidney have been described: Swelling of tubular epithelial cells with heavy fat 840,2348
content, swelling of collecting tubules of the nephrons, glomerular congestion, slight tubular 2349,450
degeneration and necrosis, diffuse degenerative changes. 1944

(3) Focal necrosis, moderate cardiac muscle fiber fatty degeneration, slight sub-endothelial 840,450
hemorrhage in the heart have been remarked. 1994,2420

(4) Skeletal muscle focal necrosis has been noted in rabbits. 840,2359,1995
450,2349

(5) Changes in the CNS: Changes in the cell bodies of spinal cord neurons have been reported. 2348,2349,1995
Cerebral and cerebellar effects have been noted. However, the CNS pathology is neither 1994,450
highly specific, characteristic, or severe. 2518,1455

(6) Pathological change of greater or lesser degree is reported for the lungs, gastrointestinal 450,1994,840,2359
tract, adrenal gland, thyroid gland and gonads. 2420,3360,398,1017

i) Symptomatology of DDT poisoning in man: [Refs.: 89,580,2066,2313,3088,1117,1739,1528,1053,667,3296,453, 1532,3199,851,1221,1821,2350]

(1) Acute intoxication: Onset in 30 minutes (20g dose), but usually 2-3 hrs or >, accompanied by paresthesia of tongue, lips, face, and, in extreme cases, arms, legs.

(2) Onset signs followed by: Sense of apprehension, equilibrium disturbances, vertigo, mental confusion and, above all, muscular tremors; convulsions, and hand paresis in severe cases. Generalized symptoms include: Malaise, fatigue, headache.

(3) Prompt vomiting may attend large doses. Delayed vomiting and/or diarrhoea are known.

(4) During stage of severe symptoms there is pupillary dilation, but reaction to light is usually normal, and nystagmus absent.

(5) Paresthetic areas show exaggerated sensitivity to touch and pain; proprioception and vibratory sensation of fingers may be lost. Coordination tends to be poor, but reflexes, save after massive doses, remain normal.

(6) Pulse irregular, and/or slowed. Blood pressure and temperature remain normal.

(7) Jaundice has been reported by one investigator.

(8) Recovery, save in very serious cases, is usually advanced or complete in 24 hours. Residual weakness of hands after heavy doses has persisted after 5 weeks.

(9) In the case of poisoning, or alleged poisoning, with insecticide formulations of DDT the picture may be greatly complicated or obscured by the presence of solvents or other agents in themselves toxic or highly irritating.

(10) Results obtained with human volunteer:
   (a) Exposure (inhalation) to 1 mg DDT/1000 ft^3, 1 hr/day for 6 days gave no untoward effects. 2350
   (b) 500 mg in olive oil, oral, gave no toxic effect.
   (c) 11 mg/k (770 mg, total) pure DDT in 25cc olive oil gave no subjective signs, tremor, twitching or abnormalities of electroencephalogram. (N.B. 11 mg/k = $\frac{1}{15}$th the LD_{50} for rat, oral.)
   (d) DDA excretion, with maximum on 2nd day, rapid decline on 3rd and 4th days, then gradual decline. 2350

j) General Summary:

(1) Massive doses yield the neurologic syndrome with initial hyper-excitibility, nervousness, eyelid twitching, progressing to severe and general tremors giving way to tonic-clonic convulsions, followed by twitchings and convulsions more prolonged, and attended by difficulties of breathing. Abrupt

culmination of the convulsive phase leaves animal exhausted and motionless. The sequence may be repeated before resolving to final, continuous and severe tremor, with coma preceding death. This general sequence was noted, with minor variations, in all 12 tested species of higher animals. Mechanical stimulus and noise will elicit the sequence; to this extent the action is strychnine-like.

- (a) Ingestion of 100 mg/k for 2 wks-5mos gave coarse tremors, resolving on withdrawal.
- (b) At 150-200 mg/k/day for 2 wks-5 mos gave severe symptoms, viz. exaggerated tremor, stretch-reflex and placing reaction; gait aberration. These also disappeared on discontinuance.

(2) Variables: Physical state of DDT, route, vehicle, maturity and nutritional state of subject, for example:

- (a) DDT in oil, oral, to Cat, Rabbit, may not produce symptoms for 60 minutes, the LD_{50} being up to 300 mg/k; intravenous in olive oil and lecithin at 40-50 mg/k, symptoms in 10 minutes, death in 1 hour.
- (b) Even in elevated dose, such vehicles as gum acacia may slow symptom onset.

(3) In chronic, sub-acute dosage, for example in the dog, effects such as hemoglobin decline with hypochromic anemia reflect a dietary cause due to prolonged appetite loss and inadequate food intake in the periods of tremor and convulsion.

3) Phytotoxicity:

a) The phytotoxic hazard, under usual conditions of use, proper application and formulation, is not high. 129
Toxicity to various Curcurbitaceae, young tomato plants and bean plants, at normal field dosages has been 2120
definitely established. Reported to be absorbed and translocated in plants when applied in lanolin and 353
polyethylene glycol.

(1) In solution culture tests on cotton seedlings, DDT and other compounds: 894

Insecticide	% Plants Damaged Beyond Recovery At Concentrations Of				
	1:100	1:1000	1:10,000	1:100,000	1:1,000,000
DDT	0	0	0	0	0
Copper aceto-arsenite	100	100	100	38.47	9.1
Tricalcium arsenite	53.85	76.93	9.1	7.7	0
Lead arsenate	100	100	33.3	0	0
Arsenomethane As-1,2-sulfide	100	70	12	10	0
Chloro- " "	100	100	100	0	0
Control	0	0	0	0	0

(2) In irrigation waters: DDT, used to kill Anopheline mosquitoes, in rice-field irrigation waters at 1 ppm 3341
DDT in emulsion formulation, is reported to do no harm to rice plants. 246

b) DDT in the soil; accumulation; hazard:

(1) Not toxic in the soil to soil bacteria, fungi or nitrifying organisms. 358,357

(2) Roots of some plants (for example, tomato, cucumber, squash, spinach, snap-beans, strawberries, and 1178
varieties of rye) were injured by excess DDT in soil. Deeply rooted plants such as trees and shrubs, 294
escaped injury; shallow rooted plants are unable to root below the zone of toxic accumulation in soil.

(3) Little effect on germination in seeds of susceptible plants, but high sensitivity after sprouting. Species 1178
and varieties vary widely in tolerance. 294

(4) Large quantities tend to accumulate in apple orchard soils but relatively small amounts in potato-fields; 1178
most is found in soil layers at plow and cultivation depths. DDT-tolerant plants have been suggested for use on soils of uprooted orchards subjected to long DDT treatment.

(5) In field tests, using soil cylinders, snap-beans, Abruzzi rye were severely stunted by purified and technical DDT at 200 lbs/acre in various mineral soils. Much less phytotoxic, at same rate, in peat soils. 3091

(6) In greenhouse tests with Black Valentine bean seedlings, DDT, at 10 ppm in nutrient solutions induced significant reduction of root growth in 10 days; purified DDT at 10 ppm completely suppressed root growth. At concentrations of < 10 ppm lateral rootlets were curtailed. Soluble phosphate in treated plants was ca. 50% that in untreated plants. 3091

- (a) Strong base anion exchange resins reduce the phytotoxicity. Wood and bone activated carbon proved effective in DDT adsorption and phytotoxicity reduction.

(7) Stability in soil: Persistent; decomposed at rate of 5% per year. At 25 lbs/acre, still effective 5 yrs. later, vs. Popillia japonica larvae. 294

- (a) Tends to remain in surface soils. At 3000 lbs/acre on undisturbed soils under large apple trees: No effect; at 50 lbs/acre among woody nursery plants: No effect. Accumulation tendency in soil is strong.
- (b) Established peach trees tolerate accumulation; seedlings damaged at 100 lbs/acre or more.
- (c) Corn, wheat, barley, oats and cereals generally (save rye) proved tolerant even to 100-400 lbs/acre in soil; rye (Abruzzi, Rosen varieties) was sensitive to 50-100 lbs/acre and 25 lbs/acre was sometimes harmful. Orchard rye, as cover crop, may be interfered with by accumulation after 4-5 years under heavy spray schedules.
- (d) Potato, cabbage, broccoli, collard, turnip, tolerated to 400 lbs/acre, tobacco tolerated to 100 lbs/acre at least; cotton, soybean, peanut proved more sensitive. Some legumes were affected at 25-50 lbs/acre; spinach, beet, tomato are highly sensitive and are damaged at 25 lbs/acre; summer squash is highly sensitive, as is pumpkin; cucumbers are moderately sensitive, muskmelon fairly tolerant; strawberries range from highly to extremely sensitive.
- (e) Not phytotoxic to tobacco following a pre-sowing spray of seedbeds at 27 lbs tech. DDT/acre or after application at 75 lbs tech. DDT/acre to 3 weeks old tobacco seedlings. 123

(8) Soil type and phytotoxicity: Acid, "mucky" soils minimize toxicity for plants injured by similar amounts on "mineral" soils. Light, sandy soils, low in silt, clay and organic matter, maximize injury for sensitive plants. Injury is diminished on "loamy" and "clayey," soils for instance, bush squash on muck showed slight harm at 400 lbs/acre; on mineral soils showed serious harm at 400 lbs/acre. 294

4) Residues, residue hazards:

a) Penetration of DDT into treated plant parts is reported for: Apple foliage and fruit, avocado foliage and fruit, citrus foliage, peach and pear fruits, coffee plants, potato foliage (various formulations used). 1298

b) Tolerance limits of 7 ppm are recommended in Great Britain. California, by law, limits residues on dried fruits and vegetables to not more than 0.049 grain DDT/lb. Commercial brushing and washing removes up to 50% of the residues on fruits and vegetables. 1298 129

c) Residue half-life: 1298

On	Initial (ppm)	14 day (ppm)	Half-life (days)	Tolerance (ppm)
Alfalfa	13	5	6	—
Citrus foliage	35	27	39	—
Citrus peel	40	25	26	7
Clover	280	125	12	—
Lettuce	80	1.3	2	7
Peach fruit	8.6	6	28	7
Peach foliage	290	125	12	—

d) For methods of determining residues consult Ref. 3199.

5) Toxicity for insects and Other arthropods:

a) DDT has been tested against so many insects of agricultural, household, and public health importance that any list is incomplete and out of date. The following list [after 1059] serves to give an idea of the range of effectiveness of DDT. (*Denotes forms against which DDT is reported ineffective.)

Apple aphid
Apple blossom weevil
Apple sawfly*
Argentine ant
Bedbug
Blister beetle
Black aphid*
Black scale
Body lice
Book lice
Bud moth
Cabbage caterpillars
Cabbage root flies
California red scale*
Carpet beetle
Carrot fly
Chafer beetle
Cherry fruit fly
Chiggers
Chinch bug
Citrus thrips
Cockroaches
Codling moth
Corn earworm
Cotton bollweevil*
Cotton bollworm
Cotton leafworm*
Crab lice
Crickets
Cucumber beetle
Corn borer
Dog fleas
Dog lice
Fall cankerworm
Fungus gnats
Grain moths
Gypsy moth
Head lice
Hog lice
Hornets
Horn flies
House flies
Human fleas
Mites (animal)
Japanese beetle
Leaf hoppers
Mexican bean beetle*
Mosquitoes
Orchard mites*
Oriental fruit moth
Pharaoh's ant*
Pea aphid
Poultry lice
Red spiders*
Sand flies
Silver fish
Southern armyworm
Spittle bugs
Spiders*
Squash bugs
Stable flies
Tarnished plant bug
Termites
Ticks
Tobacco moth
Tomato fruitworm
Tomato hornworm
Tsetse flies
Warble flies
Wasps
White-fringed beetle
Wooly Aphis*

b) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti (adult ♂)	Contact Spray	LD_{50}	5.5 (4.5-5.5) μg/g	As 0.3% DDT w/v in odorless distillate; maximum LD_{50}.	693
Aëdes aegypti (adult ♀)	Contact Spray	LD_{50}	8.0 (7.5-8.5) μg/g	" " " "	693
Aëdes aegypti (larva)	Medium	LC_{70}-LC_{100}	0.001-0.0015 ppm	Mortality as shown in 48 hrs.	476
Aëdes aegypti (larva 3rd I)	Medium	LC_{100} 48 hrs	0.05 ppm	Pure DDT (colloidal) in water.	1176
Aëdes aegypti (pupa)	Medium	LC_{50} 48 hrs	25 ppm		1176
Aëdes aegypti (")	Medium	LC_{100} 24 hrs	230 ppm		1176
Aëdes dorsalis (larva)	Medium	LC_{87} 24 hrs	1 ppm		2282
Aëdes dorsalis (pupa)	Medium	LC_{6} 24 hrs	1 ppm		2282
Aëdes dorsalis (larva)	Medium	LC_{100} 24 hrs	1 ppm	Laboratory tests at 75°F.	2283
Aëdes vexans (larva)	Medium	LC_{100} 24 hrs	1 ppm	" "	2283
Aëdes nigromaculis (4th I larva)	Medium	LC_{50} 24 hrs	0.0588 ppm	DDT-R biotypes, San Joaquin Valley, California.	1193
Aëdes aegypti (adult)		LD_{50}	5; 7 μg/g		696
Anopheles quadrimaculatus (adult) ♂	Topical	LD_{50}	0.02 μg/insect	Pure p,p'-DDT in ethanol solution.	2051
Anopheles quadrimaculatus (") ♀	Topical	LD_{50}	0.066 μg/insect	" " "	2051
Anopheles quadrimaculatus (adult) ♂	Topical	LD_{90}	0.045 μg/insect	" " "	2051
Anopheles quadrimaculatus (") ♀	Topical	LD_{90}	0.13 μg/insect	" " "	2051
Anopheles quadrimaculatus (larva)	Medium	LC_{100} 48 hr	0.03 ppm		476
Anopheles quadrimaculatus (larva)	Medium	MLC_{100}	0.01 ppm	66% mortality at 0.005 ppm.	2020
Agrotis orthogonia (larva)	Contact Spray	$LDeposit_{50}$	80 μg/cm^2		350

b) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Anthonomus grandis (adult)	Residue, or	LC_{50}	9.1 lbs/acre	As dust applied to food plant before exposure.	2276
Apis mellifera (adult)	or	LD_{50}	4.6 μg/bee	As colloidal DDT in syrup.	910
Apis mellifera (adult)	Topical	LD_{50}	114 μg/g		206
Apis mellifera (adult)	Topical	LD_{95}	224 μg/g		206
Apis mellifera (adult)	or	LD_{50}	1.7 μg/g		206
Apis mellifera (")	or	LD_{95}	14.6 μg/g		206
Apis mellifera (")	inj	LD_{50}	0.2 μg/g		206
Apis mellifera (")	inj	LD_{95}	400 μg/g		206
Apis mellifera (")	Contact Spray	LC_{20}	0.1 g/100cc	As dispersible powder, Gesarol E.	3247
Apis mellifera (")	Contact Spray	LC_{50}	0.16 g/100cc	" "	3247
Apis mellifera (")	Contact Spray	LC_{95}	0.39 g/100cc	" "	3247
Apis mellifera (")	Residual Spray	LC_{100} 24 hr	1%	Gesarol E spray.	3247
Apis mellifera (")	Residual Spray	LC_{100} 5 days	0.5%	"	3247
Apis mellifera (")	or	LD_{20} 72 hrs	5.4 mg x 10^{-3}/bee	In sugar, honey as suspension.	3247
Apis mellifera (")	or	LD_{50} 72 hrs	9.1 mg x 10^{-3}/bee	" "	3247
Apis mellifera (")	or	LD_{95} 72 hrs	25.0 mg x 10^{-3}/bee	" "	3247
Apis indica (hive)	or	LD_{96} 7 days	0.05%	DDT in $\frac{1}{4}$ oz honey fed daily to hive.	3247
Blattella germanica (adult)	Residual Dust	LD_{70} 4 days	25 μg/insect, 217 μg/g	Insects entering dusted area at will.	2181
Blattella germanica (")	Contact Spray	$LDeposit_{50}$	40 μg/cm^2		356
Blattella germanica (")	Contact Dust	$LDeposit_{50}$	15 μg/cm^2		2357
Blattella germanica (")	Environmental Dust	$LDeposit_{50}$	2.5 μg/cm^2		2357
Blattella germanica (") ♀	Topical	LD_{50} 48 hrs	13.5 μg/insect	Normal, non-R biotype.	1012
Blattella germanica (") ♀	Topical	LD_{50} 48 hrs	25.0 μg/insect	DDT-R biotype; degree resistance 1.9.	1012
Blattella germanica (") ♀	Topical	LD_{50} 48 hrs	19.0 μg/insect	Chlordane-R biotype; degree resistance 1.4.	1012
Calandra granaria (")	Residual Film	LC_{50} 120 hrs	2.67 x 10^{-6}M/cc	Oil films.	2998
Calandra granaria (")	Residual Film	LC_{95} 120 hr	12.76 x 10^{-6}M/cc	Oil films.	2998
Calandra granaria (")	Residual Film	ED_{50}	1.05 mg/cc	As oil sprays on filter paper.	2998
Calandra granaria (")	Residual Film	ED_{95}	6.61 mg/cc	" "	2998
Calliphora vomitoria (adult)	Topical	LD_{50}	9-28 μg/g	In kerosene solution.	3097
Caurasius morosus	inj	LD_{50}	60 μg/g	H_2O-oil sol. DDT emulsion.	846
Chaoborus punctipennis (larva)	Medium	MLC	13 μg/cc		2018
Chaoborus punctipennis (pupa)	Medium	MLC	26 μg/cc		2018
Choristoneura fumiferana (larva)	Contact Spray	$LDeposit_{50}$	0.3 μg/cm^2		350
Chrysops discalis (adult)	Topical	LD_{50}	20 μg/fly		2707
Chrysops discalis (")	Topical	LD_{90}	250 μg/fly		2707
Cimex lectularius (")	Contact Spray	LC_{50}	0.5%	In P31 oil, spray deposited at 0.36 mg/cm^2.	418,414
Cimex lectularius (")	Contact Spray	LC_{50}	0.56%	" " "	413
Cimex lectularius (")	Contact Spray	LD_{50}	0.25 μg/insect, 63 μg/g		413
Cimex lectularius (")	Contact Dusts	LC_{100} 24 hr	5-10%	DDT in kaolin.	413
Cirphis unipuncta (3rd instar larva)	Direct Dust	$LDeposit_{50}$ 48 hrs	0.33 μg/cm^2	Dust in pyrophyllite applied to insects, food.	299
Cirphis unipuncta (larva)	Topical	LD_{50}	193 μg/g	Ratio to parathion = 52.2; LD_{50}: LD_{99} = 3.4.	3268
Cirphis unipuncta (")	or	LD_{50}	45.7 μg/g	" 18.3; ratio LD_{50}:LD_{99} = 22.8.	3268
Culex pyrenaicus (")	Medium	MLC	0.1 mg/cc		2742
Culex tarsalis (4th instar larva)	Medium	LC_{50} 24 hr	0.111 ppm	DDT-R biotypes, San Joaquin Valley, California.	1193
Dacus dorsalis (adult)	Topical	LD_{50}	0.23 μg/fly		2692
Diataraxia oleracea (larva) final I	Contact Spray	LD_{50}	0.47 μg/larva	Body weight of larva 0.24 g.	3245
Diataraxia oleracea (") "	Contact Spray	LD_{50}	1.6 μg/larva	" 0.34 g.	3245
Diataraxia oleracea (") "	Contact Spray	LD_{50}	4.1 μg/larva	" 0.44 g.	3245
Diataraxia oleracea (") "	Contact Spray	LD_{50}	8.7 μg/larva	" 0.54 g.	3245
Diataraxia oleracea (") "	Contact Spray	LD_{50}	24.0 μg/larva	" 0.71 g.	3245
Diataraxia oleracea (") "	or	LD_{50}	4.5 μg/larva	" 0.32 g; on leaves.	3245
Diataraxia oleracea (") "	or	LD_{50}	12.0 μg/larva	" 0.42 g; "	3245
Diataraxia oleracea (") "	or	LD_{50}	33.0 μg/larva	" 0.56 g; "	3245
Ephestia kühniella	Medium	LC_{50}	860 ppm	Mixed with stored cereals.	353
Fannia canicularis (adult) ♀	Topical	LD_{50} 24 hrs	2.80 μg/fly	Av. wgt 7.35 mg; measured drop method; in acetone.	1981
Fannia canicularis (") ♂	Topical	LD_{50} 24 hrs	1.3 μg/fly	" 6.89 mg; " "	1981
Galleria mellonella (larva)	or	LD_{50}	151 μg/g		206
Galleria mellonella (")	or	LD_{95}	991 μg/g		206
Galleria mellonella (")	inj	LD_{50}	74.2 μg/g		206
Galleria mellonella (")	inj	LD_{50}	210 μg/g		206
Heliothis ononis (")	Contact Spray	$LDeposit_{50}$	7 μg/cm^2		350
Heliothis virescens (larva, 6th instar)	Topical	LD_{50}	6.5 mg/g	250-450 mg. body wgt; in methylethyl ketone.	1124
Heliothis zea (larva, 6th instar)	Topical	LD_{50}	3.0 mg/g	" " "	1124
Locusta migratoria migratorioides (adult)	Topical	LD_{50} 5 days	140.0 μg/locust ± 7.6; 133 μg/g	In tractor oil + cyclohexanone 9:1.	1585
Locusta migratoria migratorioides (adult)	Topical	LD_{95} 5 days	258.0 ± 18.6 μg/locust; 245 μg/g	" "	1585
Melanoplus differentialis (adult)	Topical	LD_{80}	9380 μg/g	Solution in organic solvents.	3267
Melanoplus differentialis (")	or	LD_{50}	> 1350; 2579 μg/g	As deposit on leaves.	3267
Melanoplus differentialis (")	or	LD_{50}	1170 μg/g	As colloidal suspension; directly applied to mouthparts.	3267
Melanoplus differentialis (")	or	LD_{50}	> 50 μg/g		1756
Musca domestica (larva)	Medium	LC_{50}	700 ppm	Mixed in the rearing medium.	351
Musca domestica (")	Medium	LC_{50}	2300 (1600-3300) ppm	Measured as % emergence compared to controls.	666
Musca domestica (adult)	Contact Spray	LC_{50} 24 hrs	0.35 mg/cc	KD 10 min = 0 at LC_{50}; turntable-Peet-Grady method.	2033
Musca domestica (")	Space Spray	LC_{50} 24 hrs	0.361 ± .037 mg/cc	As kerosene space spray.	2365
Musca domestica (")	Space Spray	LC_{50} 24 hrs	0.24 mg/cc	Mean LC_{50}; Campbell's Turntable Method.	2364
Musca domestica (")	Space Spray	LC_{50}	0.788 mg/cc	Turntable Method.	1156
Musca domestica (")	Topical	LD_{50} 24 hrs	0.033 μg/fly	Acetone sol.; measured drop method.	1981,2692
Musca domestica (")	Topical	LD_{50} 24 hrs	0.02 μg/fly	DDT-non R biotype; measured drop method.	78
Musca domestica (")	Topical	LD_{50} 24 hrs	0.5 μg/fly	DDT-R biotypes, Riverside and Ontario.	78
Musca domestica (")	Topical	LD_{50} 24 hrs	0.7 μg/fly	DDT-R biotype, San José.	78
Musca domestica (")	Topical	LD_{50} 24 hrs	10.0 μg/fly	DDT-R biotype, Bellflower.	78
Musca domestica (")	Topical	LD_{50}	7.4 μg/fly	" "	1591
Musca domestica (")	Topical	LD_{50}	0.05 μg/fly	" , Berkeley.	1591
Musca domestica (")	Topical	LD_{50}	0.5 μg/fly	" , Laton.	1591
Musca domestica (")	Topical	LD_{50}	2.5 μg/fly	" , Super Laton.	1591
Musca domestica (") ♀	Topical	LD_{50}	0.12 μg/fly	DDT-non R biotype, Laboratory.	1803
Musca domestica (") ♀	Topical	LD_{50}	8.3 μg/fly	DDT-R biotype, Bellflower.	1803

Insect	Route	Dose	Dosage	Remarks	
Musca domestica (adult) ♀	Topical	LD_{50}	12.3 µg/fly	DDT-R biotype, Orlando.	1803
Musca domestica (adult, newly emerged)	Topical	LD_{50}	2 µg/g	In acetone solution.	3097
Musca domestica (adult mature)	Topical	LD_{50}	8-21 µg/g	"	3097
Musca domestica (adult ♀)	Topical	LD_{50}	9 µg/g	"kerosene " .	693
Musca domestica (" ♂)	Topical	LD_{50}	6 µg/g	"kerosene " .	693
Musca domestica (adult)	Topical	LD_{50}	7; 10 µg/g		696
Musca domestica (adult)	Topical	LD_{50} 24 hrs	16.8 µg/g	NAIDM DDT-non R biotype Lab. I in acetone.	373
Musca domestica (")	Topical	LD_{50} 24 hrs	8.96 µg/g	U. of Indiana DDT-non R biotype Lab II in acetone.	373
Musca domestica (") DDT-I	Topical	LD_{50} 24 hrs	13,040.1 µg/g	DDT-R; origin Lab I, 21 generations selection.	373
Musca domestica (") DDT-W	Topical	LD_{50} 24 hrs	505.5 µg/g	" " Field, 3 yrs exposure in field to DDT.	373
Musca domestica (") DDT-III	Topical	LD_{50} 24 hrs	1350.0 µg/g	" " " 4 yrs "	373
Musca domestica (") Methoxy-I	Topical	LD_{50} 24 hrs	19.2 µg/g	Methoxychlor-R; origin Lab I; 21 gen. selection.	373
Musca domestica (") Lindane-I	Topical	LD_{50} 24 hrs	18.2 µg/g	Lindane-R; origin Lab I; 21 gen. selection.	373
Musca domestica (") Multi-I	Topical	LD_{50} 24 hrs	18,728.0 µg/g	Multi-insecticide R; origin DDT I; 8 gen. further selection.	373
Musca domestica (") Dieldrin-I	Topical	LD_{50} 24 hrs	15.1 µg/g	Dieldrin-R; origin Lab I; 21 gen. selection.	373
Musca domestica (") Chlordane-I	Topical	LD_{50} 24 hrs	16.2 µg/g	Chlordane-R; " "	373
Musca domestica (") Pyro-I	Topical	LD_{50} 24 hrs	34.7 µg/g	Pyrethrin-R; " "	373
Musca domestica (") Multi-III	Topical	LD_{50} 24 hrs	135.1 µg/g	Multi-insecticide R; origin Methoxy-I 8 gen. selection.	373
Musca domestica (") Multi-IV	Topical	LD_{50} 24 hrs	18.8 µg/g	" " 4 "	373
Musca domestica (") Multi-II	Topical	LD_{50} 24 hrs	20.0 µg/g	" " 4 "	373
Musca domestica (") Orlando Spec.	Residues	$LTime_{70}$	230 minutes	Residues at 25 mg/ft^2; DDT-R biotype.	1803
Musca domestica (") Bellflower	Residues	$LTime_{70}$	184 minutes	" "	1803
Musca domestica (") Laboratory	Residues	$LTime_{70}$	3.2 minutes	" ; DDT-non R biotype.	1803
Musca domestica (") Non-R	Residues	$LTime_{50}$	9.0 minutes		3320
Musca domestica (") Orlando-I	Residues	$LTime_{50}$	ca 1440 minutes	DDT-R biotype.	3320
Musca domestica (") LDD	Residues	$LTime_{80}$	>240 minutes	"	3320
Musca domestica (") Ballard	Residues	$LTime_{50}$	343.4 minutes	"	3320
Oncopeltus fasciatus	Topical	LD_{50}	409 µg/g		206
Oncopeltus fasciatus	Topical	LD_{95}	8280 µg/g		206
Oncopeltus fasciatus	or	LD_{50}	301 µg/g		206
Oncopeltus fasciatus	or	LD_{95}	1966 µg/g		206
Oncopeltus fasciatus ♂ ♀	Dipping	LD_{50}	10 µg/cc	DDT-non R biotype; unselected.	1329
Oncopeltus fasciatus ♂ ♀	Dipping	LD_{50}	37 µg/cc	Selected 17 generations vs. DDT.	1329
Oncopeltus fasciatus (adult ♀)	inj	LD_{50} 24 hrs	31 µg/g	Calculated from regression equations, 3 replicates, 5700 insects.	348
Oncopeltus fasciatus (" ")	inj	LD_{50} 48 hrs	11 µg/g	" " "	348
Oncopeltus fasciatus (" ")	inj	LD_{95} 24 hrs	1043 µg/g	" " "	348
Oncopeltus fasciatus (" ")	inj	LD_{95} 48 hrs	437 µg/g	" " "	348
Pediculus humanus corporis	Contact Spray	LC_{50}	0.3%	In P31 oil; spray deposited at 0.36 mg/cm^2.	418,414
Pediculus humanus corporis	Contact Spray	LD_{50}	0.054 µg/insect; 27 µg/g		413
Pediculus humanus corporis	Contact Dust	LC_{100} 24 hrs	5-10%	DDT in kaolin.	413
Periplaneta americana	Contact Dust	LD_{70} 10 days	37 µg/insect; 36 µg/g	Entering treated area at will.	2181
Periplaneta americana ♂ (adult)	inj	LD_{50} 96 hrs	4.5 µg/g	In xylene, acetone, deobase, ethanol 10:10:75:5.	558
Periplaneta americana ♀ (")	inj	LD_{50} 96 hrs	20.0 µg/g	" " "	558
Periplaneta americana ♂ (")	inj	LD_{0}	2 µg/g	Av. wgt 0.9 (0.7-1.15)g.	2219
Periplaneta americana ♀ (")	inj	LD_{0}	10 µg/g	" 1.3 (1.0-1.9)g.	2219
Periplaneta americana ♂ (")	inj	LD_{50}	8 µg/g		2219
Periplaneta americana ♀ (")	inj	LD_{50}	20 µg/g		2219
Periplaneta americana ♂ (")	inj	LD_{100}	20µg/g		2219
Periplaneta americana ♀ (")	inj	LD_{100}	40 µg/g		2219
Periplaneta americana ♂ (")	inj (intra-abd.)	LD_{50}	5-8 µg/g	In acetone solution.	3097
Periplaneta americana ♀ (")	inj (")	LD_{50}	18 µg/g	Lecithin-peanut oil emulsion.	3097
Periplaneta americana ♂ (")	inj (")	LD_{50}	82 µg/g	In peanut oil.	3097
Periplaneta americana (adult)	Topical	LD_{50} 5 days	5-10 µg/insect	In dioxane; at 15°C post-treatment.	3189
Periplaneta americana (")	Topical	LD_{50} 5 days	75-100 µg/insect	In dioxane; at 35°C post-treatment.	3189
Periplaneta americana (")	Injection	LD_{50} 5 days	2-3 µg/insect	" 15°C "	3189
Periplaneta americana (")	Injection	LD_{50} 5 days	20-25 µg/insect	" 35°C "	3189
Periplaneta americana (adult)	inj	LD_{50}	20 µg/g	In water-oil emulsion.	846
Periplaneta americana (")	Topical	LD_{50}	10 µg/g	In acetone solution.	3097
Periplaneta americana (")	Contact Spray	MLC	0.01 mg/cc	In water suspension.	2688
Popillia japonica	Topical	LD_{50}	93 µg/g		206
Popillia japonica	Topical	LD_{95}	549 µg/g		206
Popillia japonica	or	LD_{50}	205 µg/g		206
Popillia japonica	or	LD_{95}	1120 µg/g		206
Popillia japonica	inj	LD_{50}	162 µg/g		206
Popillia japonica	inj	LD_{95}	679 µg/g		206
Prodenia eridania (large larvae)	or	LD_{50}	31 µg/g	By the leaf sandwich method.	3017
Protoparce sexta (larva, 5th instar)	Topical	LD_{50}	≫4000 µg/larva	Av. wgt. larva 5.4 (4.1-7.5)g.	1306
Protoparce sexta (larva, 3rd, 4th instar)	Topical	LD_{50}	2344 µg/larva	" 2.5 (1.2-4.0)g.	1306
Protoparce sexta (")	Topical	LD_{90}	9897 µg/larva	" "	1306
Protoparce sexta (" 2nd, 3rd ")	Topical	LD_{50}	366 µg/larva	" 0.9 (0.6-1.1)g.	1306
Protoparce sexta (")	Topical	LD_{90}	1342 µg/larva	" "	1306
Protoparce sexta (larva, 5th instar)	or	LD_{50}	4416 µg/larva	" 5.4 (4.1-7.5)g.	1306
Protoparce sexta (")	or	LD_{90}	28,040 µg/larva	" "	1306
Protoparce sexta (" 2nd, 3rd instar)	or	LD_{50}	15.8 µg/larva	" 0.9 (0.6-1.1)g.	1306
Protoparce sexta (")	or	LD_{90}	1125 µg/larva	" "	1306
Simulium damnosum (larva)	Medium	LC_{100}	0.1 ppm	As xylene + triton emulsion in flowing stream.	958
Sitophilus granarius	Medium	LC_{50}	16 ppm	Mixed with stored grain.	353
Sitophilus granarius (adult)	Dry Residues	ED_{100}	0.11 mg/7 cm diameter filter paper	Deposited on paper from acetone.	2999
Sitophilus granarius (")	Oil Film Residues	EC_{25}	96 hrs 0.4 mg/cc	In P31 oil deposited + diffused on filter paper.	2999
Sitophilus granarius (")	"	EC_{50}	96 hrs 0.81 mg/cc	" "	2999
Sitophilus granarius (")	"	EC_{95}	96 hrs 4.74 mg/cc	" "	2999
Sitophilus granarius (")	"	EC_{50}	96 hrs 2.66 (2.06-3.43)mg/cc	" "	2999
Tribolium confusum	Medium	LC_{50}	16 ppm	Mixed with stored dry grain.	353
Tribolium castaneum (adult)	Contact Spray	LC_{50}	0.95% w/v	In Wakefield half-white oil; at 80°F post-treatment.	2532
Tribolium castaneum (")	Contact Spray	LC_{50}	0.36% w/v	" 65°F "	2532
Theobaldia longeareolata (larva)	Medium	MLC	0.02 mg/cc	In water environment of larvae.	2742
Drosophila melanogaster (adult)	Contact Spray	LC_{50}	0.088 mg/l	Wild biotype sprayed with 0.015% suspension.	3057
Drosophila melanogaster (")	Contact Spray	LC_{50}	0.176 mg/l	Exposed to DDT sprayings.	3057
Drosophila melanogaster (")	Contact Spray	LC_{50}	0.304 mg/l	Exposed to DDT; selected for 6 generations.	3057

c) Comparative toxicity DDT, and other compounds:

(1) Toxicity of DDT isomers (variation in position of Cl on aromatic rings): 418,646,3288

Isomer	As 1% In Refund Kerosene At 1 cc/100 ft³ Vs.						LC₅₀ (% Conc. w/v) Contact Spray in Oil Vs.	
	Musca domestica			Anopheles quadrimaculatus				
	KD 10 min (%)	KD 30 min (%)	Kill 24 hrs (%)	KD 10 min (%)	KD 30 min (%)	Kill 24 hrs (%)	Pediculus humanus	Cimex lectularius
o,o'-DDT	0	0	1	5	6	15	— *	— *
p,p'-DDT	0	14	50	20	69	89	0.3	0.53
o,p'-DDT	0	0	0	6	8	20	5.5	20.0

*Virtually non-toxic for Pediculus, Cimex.

(2) Relative toxicity of DDT-isomers: 2637

Anopheles quadrimaculatus (larva) p,p' = 1.0, m,p' = 0.5, o,p' = 0.17, o,o' = 0.0013
Musca domestica (adult) p,p' = 1.0, m,p' = 0.9, o,p' = 0.018, o,m' = <0.015, o,o' = <0.01

(3) Comparative toxicity DDT-isomers and isomer combinations, for Anopheles quadrimaculatus, 4th instar larva: 1724

Isomer/Isomer Combination	Average % Mortality At Concentration Shown (ppm)													
	.000125		.0025		.005		.0075		.01		.02		.03	
	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr
p,p'-DDT	4.6	12.9	9.3	15.6	44.7	55.3	—	—	94.2	97.4	—	—	—	—
o,p'-DDT	—	—	—	—	1.0	3.5	—	—	4.2	10.7	19.0	34.8	40.6	58.6
o,p + p,p' 3:1	—	—	—	—	4.0	11.0	15.4	28.3	33.4	57.2	—	—	—	—
o,p' + p,p' 1:1	—	—	3.5	12.1	24.3	37.2	51.2	63.8	71.5	84.5	—	—	—	—
o,p' + p,p' 1:3	0	3.4	2.0	3.9	30.0	41.8	69.6	80.8	85.0	89.0	—	—	—	—

(4) DDT, (p,p'-isomer) other compounds vs. 4 day old adult Anopheles quadrimaculatus. By topical application in ethanol solution: 2051

Insecticide	LD₅₀ (μg/insect)		LD₉₀ (μg/insect)	
	♂	♀	♂	♀
p,p'-DDT	0.02	0.066	0.045	0.13
p,p'-DDD	.041	.1	.098	.22
Methoxychlor (tech)	.035	.1	.078	.22
Chlordane	.105	.24	.19	.46
Dieldrin	.009	.023	.022	.048
Lindane	.0085	.011	.032	.042
Toxaphene	.15	.29	.29	.5
Malathion	.0087	.0095	.019	.022
Allethrin	.0029	.008	.013	.041

Relative Effectiveness Compared to DDT				
Insecticide	At LD₅₀		At LD₉₀	
	♂	♀	♂	♀
Toxaphene	0.13	0.23	0.16	0.26
Chlordane	0.19	0.28	0.24	0.28
p,p'-DDD	.49	.66	.46	.59
Methoxychlor	.57	.66	.58	.59
p,p'-DDT	1.0	1.0	1.0	1.0
Dieldrin	2.2	2.9	2.0	2.7
Lindane	2.4	6.0	1.4	3.1
Allethrin	6.9	8.3	3.5	3.2
Malathion	2.3	7.0	2.4	5.9

(5) DDT and other compounds vs. adult Aëdes aegypti: As contact sprays; DDT and BHC as 0.3% w/v in 1:1 odorless distillate + benzene, pyrethrins as 0.1% ω/ν in the same solvent:
Maximum LD₅₀ (μg/g) DDT = (♂) 5.5 (4.5-5.5) (♀) 8.0 (7.5-8.5) BHC = (♂) 3.0, (♀) 3.5, pyrethrins = (♂) 0.5 (0.5-1.0) (♀) 1.0 (1.0-1.5).

(6) DDT and other compounds vs. DDT-R field biotypes (San Joaquin Valley, California); 4th instar larvae, laboratory tests: 1193

Insecticide	LD₅₀ (ppm) For	
	Aëdes nigromaculis	Culex tarsalis
DDT	0.0588	0.111
EPN®	.000862	.000649
NPD	.0625	.0178
Malathion	.025	.0185

(7) DDT and other chlorinated hydrocarbons vs. Aëdes dorsalis and Aëdes vexans larvae and pupae. Laboratory tests at 75°F in distilled water: 2283 2282

Insecticide	% Mortality (24 hrs) At						
	1 ppm		.5 ppm		.2 ppm		.1 ppm
	larvae	pupae	larvae	pupae	larvae	pupae	larvae
DDT	100	6	96.9	30	100	8.2	98
Aldrin	100	75	96.9	30.4	99	34	95
Dieldrin	100	79	96.9	78	99	63	95
Endrin	100	95	98.9	99	98	61	98
Isodrin	100	78.8	98	70	97	58	81
Toxaphene	96	—	93	2.3	91	2.7	84
Control	15.2	2.4	—	—	—	—	—

(8) DDT and organic phosphate insecticides vs. Anopheline mosquito larvae. Laboratory and field tests: 1766

Insecticide	Laboratory								Field								
	Anopheles quadrimaculatus 4th instar % Mortality, 48 hrs at (ppm)								A. quadrimaculatus, A. crucians % Kill, 24 hrs at (lbs/acre)								
	0.1	0.05	0.025	0.01	0.005	0.0025	0.001	0.005	0.25	0.1	0.05	0.025	0.01	0.005	0.0025	0.001
DDT	—	—	—	100	94	49	24	—	—	—	99	98	99	98	95	92
Sulfotepp	100 ————————						74	34	—	85	72	73	63	53	30	—
Parathion	100 ———————					96	56	34	—	—	97	97	92	99	88	—
EPN®	100 ———————					96	32	—	—	—	95	96	96	95	92	91
Methyl parathion	100 ———————					67	—	—	—	100	98	83	69	51	50	—
Chlorthion analogue*	100 ————			96	86	62	62	44	—	99	72	78	49	30	—	—
Malathion	100 ——		96	80	80	60	40	24	90	78	79	68	60	—	—	—
EPN analogue**	100 ——————				70	80	4	—	—	99	80	88	75	70	69	71
Diazinon	100 ——————				36	20	—	—	—	97	97	79	58	65	55	53
Para-oxon	100 ————			82	50	—	—	—	—	90	77	54	46	45	49	31
Bayer 21/199	100 ————			64	46	24	—	—	—	—	98	98	99	96	91	84
Chlorthion	100 ——		88	76	44	—	—	—	100	99	82	73	57	50	—	—
Potasan	100	98	56	30	5	—	—	—	—	77	59	72	52	—	—	—
"DPT"***	100	94	58	26	—	—	—	—	—	—	78	64	75	74	45	35
NPD	94	—	62	30	—	—	—	—	100	97	84	87	79	—	—	—

* = O,O-dimethyl-O-(2-chloro-4-nitrophenyl thiophosphate; ** = Ethyl o-nitrophenyl thionobenzene phosphonate.
*** = O,O-diethyl-O-piperonyl thiophosphate.

(a) For anopheline larvae toxic field concentrations, as 5% oil solutions, are reported to be 0.1-0.4 lb DDT/acre of water surface. Adult anophelines are killed at 2-3 quarts/acre of 5% oil solutions sprayed by air over dense vegetation. 2948

(b) Anopheles albimanus (adults) eliminated by 0.4 lb DDT/acre as a 10% spray applied over jungle forests. 2948

(c) As a residual spray at 200 mg DDT/ft^2 protection against Anopheles quadrimaculatus and various other anophelines was conferred for >70 days. 2948

(d) Mortality in groups of 20 Anopheles quadrimaculatus, early 4th instar larvae, exposed in 100cc distilled water at 64°F-78°F to various amounts of p,p'-DDT.

Exposure Time (hrs)	Average % Mortality At µg DDT/cc Shown						
	2.0	0.5	0.2	0.05	0.02	0.005	0.002
24	94.96± 8.26	80.64± 20.02	73.7 ± 17.23	41.89± 27.89	28.29± 22.03	4.95± 5.29	3.39± 5.18
48	100 ± 0.0	99.07± 2.21	95.91± 4.98	67.16± 25.42	52.11± 32.09	15.07± 20.25	10.38± 16.06

(9) DDT and other compounds vs. Anthonomus grandis; combined oral and contact action of dusts applied to cotton plants before exposure of the test insects; LD$_{50}$ given in lbs/acre of active ingredient: DDT = 9.1, Dieldrin = 0.9, Aldrin = 1.1, BHC (tech) = 1.0, Chlordane = 10.1, Toxaphene = 6.4, Prolan = 11.4, Bulan = 16.7 2276

(10) DDT and other compounds vs. Periplaneta americana and Blattella germanica:

(a) 356,2357,2181

Insecticide	Blattella germanica LDeposit$_{50}$ (µg/cm^2)			LD$_{70}$ 10 days Environmental Dust*			
				B. germanica		Periplaneta americana	
	Direct Spray	Direct Dust	Environmental Dust	(µg/insect)	(µg/g)	(µg/insect)	(µg/g)
DDT	40	15	2.5	25	217	37	36
Chlordane	1.7	2.0	0.6	—	—	—	—
Lindane	2.8	0.8	0.2	3.6	31	72	69
Pyrethrins	—	—	—	5	43	10.8	10.4
Sodium fluoride	—	130	40	158	1375	1833	1763

*Insects entering the treated area at will; pyrethrins yielded the highest KD 1 hour followed in turn by lindane and DDT.

(b)

Vs. non-R, DDT-R and Chlordane-R biotypes of Blattella germanica. Topical application to adult ♀ insects: 1012

Insecticide	LD$_{50}$ 48 Hours (µg/insect)				
	Non-R	DDT-R	Degree Resistance	Chlordane-R	Degree Resistance
DDT	13.5	25.0	1.9	19.0	1.4
Chlordane	2.3	4.1	1.8	250.0	108.6
Dieldrin	0.5	0.62	1.2	34.0	68
Diazinon	0.33	0.78	2.4	0.4	1.2
Allethrin (synergized)	0.76	1.3	1.7	1.0	1.3

(c)

Vs. Periplaneta americana adults. Injection, as solutions in xylene + acetone + Deobase Oil + ethanol (10: 10: 75: 5): 558

Insecticide	LD_{50} 96 Hrs (µg/g)		LD_{50} ♀ / LD_{50} ♂
	♂	♀	
DDT*	4.5	20	4.4
Lindane	0.8	4.4	5.5
Dieldrin	1.0	5.0	5
Toxaphene	25.0	80.0	3.2
Chlordane	26.0	52.0	2.0
Methoxychlor	7.0	18.0	2.5

*No discernible differences noted in susceptibility to DDT between adult ♀ and ♂ nymphs or ♀ nymphs (last instar).

(d)

Vs. P. americana. Injection: 2219

Insecticide	Amount As µg/g To Yield Mortality (%) Shown					
	0%		50%		100%	
	♂	♀	♂	♀	♂	♀
DDT	2	10	8	20	20	40
Nicotine (alkaloid)	30	80	80	120	140	200
Pyrethrins I, II	1	5	3	8	6	11
Derris (rotenone 25%)	3	5	5	8	9	13
Sodium arsenate	23	35	30	50	45	70
Acid lead arsenate	200	300	300	750	750	1400
Lethane® 384	100	120	150	200	200	400
Sodium fluoride	80	100	120	140	150	170
Azobenzene	320	500	430	620	570	820
Sodium 4,6-dinitro-o-cresylate	7	20	14	28	21	50

(11) DDT and other compounds vs. several species of Diptera; adult insects: 2707, 1981, 2033, 2692

Insecticide	Chrysops discalis (µg/fly) Topical		Fannia canicularis** LD_{50}, Topical (µg/fly) 24 hrs		Dacus dorsalis LD_{50} Topical (µg/fly)	Rhagoletis completa LD_{50} Topical µg/fly	Musca domestica		
	LD_{50}*	LD_{90}	♀	♂			LD_{50} 24 hr*** Topical µg/fly ♀	LC_{50} 24 hr**** Contact Spray µg/cc	%KD 10 min Contact Spray at LC_{50} 24 hr
DDT	20	250	2.8	1.3	0.23	0.86	0.033	350	0
Lindane	4	35	0.76	0.39	0.025	0.027	0.01	46	0
Endrin	9	80	—	—	—	—	—	—	—
Dieldrin	20	950	0.003	0.0026	0.024	0.025	0.031	17	0
Methoxychlor	30	90	0.14	0.12	1.0	0.15	0.068	—	—
Aldrin	40	170	—	—	0.023	0.066	0.035	56	0
Heptachlor	40	200	—	—	0.015	0.06	0.032	52	0
EPN®	48	120	—	—	—	—	—	—	—
Isodrin	60	170	—	—	—	—	—	—	—
Chlordane	60	650	—	—	—	—	—	250	—
Chlorthion	65	420	0.035	0.022	—	—	0.33	—	—
Diazinon	90	360	0.098	0.054	—	—	0.092	—	—
Bayer 21/199	90	910	—	—	—	—	—	—	—
Q-137	120	400	—	—	—	—	—	—	—
Malathion	130	330	0.10	0.06	—	—	0.56	480	0
Toxaphene	180	480	—	—	—	—	—	680	0
DDD	—	—	—	—	>1.0	0.18	0.13	—	—
Parathion	—	—	—	—	0.012	0.011	0.015	20	0
Methyl parathion	—	—	—	—	—	—	—	25	0
TEPP	—	—	—	—	—	—	—	69	ca70
NPD	—	—	—	—	—	—	—	69	0
Dilan	—	—	—	—	—	—	—	720	ca30
Isolan	—	—	—	—	—	—	—	1150	100
Allethrin	—	—	—	—	—	—	—	1500	100
Pyrethrins	—	—	0.24	0.44	—	—	1.0	—	—
Pyrolan	—	—	—	—	—	—	—	5500	100

*= Estimated from dose-mortality curves. ** = 3 day old laboratory-reared adults, average weight ♂ = 6.89 mg, ♀ 7.35 mg; insecticides in acetone solution, measured drop method. *** = Insecticides in acetone solution, measured drop method. **** = Contact sprays applied by a turntable modification of Peet-Grady Method.

(12) DDT and other compounds vs. *Musca domestica* larvae 3rd Instar. Toxicants incorporated in the larval rearing medium. Mortality measured by % pupal emergence compared with control: 666

Insecticide	LC_{50} (ppm)	Fiducial Limits (0.95 Level)	
DDT	2300	1600-3300	
Endrin	125	100- 160	
Aldrin	430	340- 595	Difference Not Significant.
Dieldrin	450	355- 595	
Chlordane	1450	1100-1900	

a) As emulsion, 2.5%-5.0% DDT yields 100% control of maggots in latrines under heavy breeding conditions in 24-72 hrs; 4-5% solutions in Diesel or fuel oil, kerosene, yield similar results; both formulations at 1 qt/seat hole. 3115

(13) DDT and its bromine, fluorine, and other analogues compared with other insecticides vs *Musca domestica* adults. Kerosene space sprays applied by Campbell's Turntable Method: Grouping of several experiences: 2365 2364 1158

Insecticide	Concentration (mg/cc) (I)	Concentration (mg/cc) (II)	KD 25 min. (%) (I)	KD 25 min. (%) (II)	% Mortality 24 hrs (I)	% Mortality 24 hrs (II)	LC_{50} (mg/cc) (I)	LC_{50} (mg/cc) (II)	Relative Toxicity At 50% Mortality Level (I)	Relative Toxicity At 50% Mortality Level (II)
DDT	1.0		49		95					
"	.667	.667	37	40	83	92	0.361	0.24	1.0	1.0
"	.444	.444	20	35	58	84	±			
"	.296	.222	42	24	43	45	.037			
Bromine-DDT	1.0		34		91		0.45		0.53	
"	0.667		29		72					
"	0.444		18		49					
Fluorine-DDT	1.5		44		82		0.82		0.29	
"	1.0		40		56					
"	0.667		26		39					
Methoxychlor	1.5		100		82		0.603 ± .062		0.6	
"	1.0		99		72					
"	0.667		98		52					
"	0.444		69		40					
DDD	2.25		95		68		1.43 ± .15		0.25	
"	1.5		90		59					
"	1.0		65		27					
"	0.667		62		16					
Parathion	0.1		—		81		0.0483			
"	0.075		—		77					
"	0.056		—		60					
"	0.042		—		48					
NPD	1.78		—		72		0.904			
"	1.33		—		61					
"	1.0		—		52					
"	0.75		—		45					

Insecticide	Concentration (I)	Concentration (II)	Concentration (III)	KD (I)	KD (II)	Mortality (I)	Mortality (II)	Mortality (III)	LC_{50} (I)	LC_{50} (II)	LC_{50} (III)	Relative Toxicity (II)
Pyrethrins	8.0		7.5	100		80		86	2.44	2.04	3.08	0.12
"	4.0	3.66	3.75	100	100	64	73	52	±			
"	2.0	1.83	1.875	100	100	42	39	24	.49			
"	1.0	0.92	0.938	100	100	28	23	15				

(14) DDT and other compounds vs. *Phaenicia sericata* adults exposed to residues on paper: 2692

Insecticide	Concentration ($\mu g/cm^2$)	KD 24 hrs (%)	Mortality 24 hrs (%)
DDT	1.0	61	44
"	0.1	21	21
"	0.01	22	11
Heptachlor	0.1	100	70
"	0.01	70	22
"	0.001	5	5
Chlordane	0.1	95	58
"	0.01	42	11
"	0.001	0	0

(15) DDT and other compounds vs. various larval lepidoptera: 3268,299

(a) Vs. *Cirphis unipuncta* larva:

(a) Vs. Cirphis unipuncta larva: 3268,299

Insecticide	LD$_{50}$ (µg/g) Topical	LD$_{50}$ (µg/g) Oral*	Ratio LD$_{50}$: LD$_{99}$ Topical	Ratio LD$_{50}$: LD$_{99}$ Oral	Lethal Deposit$_{50}$** 48 hrs (µg/cm^2) For 3rd Instar Larvae
DDT	193	45.7	4.7	22.8	0.35
DFDT	—	—	—	—	0.33****
Chlordane	117.5	78.2	4.9	4.7	—
Toxaphene®	56.2	34.1	4.7	2.9	—
Lindane	28.1	27.9	3.2	5.1	0.16
Aldrin	19.8	11.4	3.7	24.7	—
Dilan	8.8	11.5	5.4	5.0	—
Dieldrin	8.3	4.6	3.1	3.8	—
Parathion***	3.7	2.5	3.4	8.5	—

*Administered on treated leaves. **Both food and insects dusted with toxicant in pyrophyllite. ***Gives fastest kill followed, in order, by dilan, lindane, DDT. ****Highest kill obtained in 48 hrs with bromine analogue at 10 µg/cm^2 = 38%.

(b) Vs. Protoparce sexta and Diataraxia oleracea: S = small larvae, 2nd or 3rd instar av. wgt. 0.9 (0.6-1.1)g; M = medium larvae, 3rd or 4th instar av. wgt. 2.5 (1.2-4.0)g, L = large larvae, 5th instar, av. wgt. 5.4 (4.1-7.5)g. 1306 3245

Insecticide	Protoparce sexta (µg/larva) LD$_{50}$ Topical L	LD$_{50}$ Topical M	LD$_{50}$ Topical S	LD$_{90}$ Topical L	LD$_{90}$ Topical M	LD$_{90}$ Topical S	LD$_{50}$ Oral L	LD$_{50}$ Oral M	LD$_{50}$ Oral S	LD$_{90}$ Oral L	LD$_{90}$ Oral M	LD$_{90}$ Oral S	Diataraxia oleracea LD$_{50}$ Oral*(µg/larva) At Larval Wgt 0.32g	0.42g	0.56g
DDT	≫4000	2334	366	—	9887	1342	4416	—	15.8	28040	—	1125	4.5	12	33
Endrin	42	2.9	0.51	219	6.3	6.3	9.9	—	0.11	49	—	0.85	—	—	—
Parathion	52	9.9	2.8	183	64	12.3	15.7	—	—	54	—	—	2.6	3.4	4.6
Isodrin	87	7.6	3.0	490	29	56	15.3	—	1.1	138	—	3.1	—	—	—
Lindane	206	—	—	1235	—	—	209	—	—	398	—	—	13.0	26.0	59.0
Malathion	481	61	23.6	1276	553	92	365	—	—	1621	—	—	—	—	—
TEPP	—	—	—	—	—	—	—	—	—	—	—	—	43.0	69.0	112
Dieldrin	482	—	—	2559	—	—	—	—	—	—	—	—	—	—	—
Aldrin	487	—	—	1359	—	—	—	—	—	—	—	—	—	—	—
Heptachlor	1058	—	—	4005	—	—	—	—	—	—	—	—	—	—	—
Toxaphene®	1363	32	30	5778	138	112	143	—	—	6025	—	—	—	—	—
DDD	2622	376	37	9813	2620	367	878	—	22.5	3192	—	58	—	—	—
Lead arsenate	—	—	—	—	—	—	—	—	—	—	—	—	66.0	78.0	91.0

*Administered by the leaf method; leaves treated in settling tower with insecticides in acetone solution, save for lead arsenate which was in water solution. LD$_{50}$ by contact spray at various larval wgts. (last instar larvae): 0.24g-0.47µg/larva; 0.34g-1.6µg/larva; 0.44g-4.1µg/larva; 0.54g-8.7µg/larva; 0.71g-24µg/larva.

(c) Vs. Prodenia eridania larva: 3017

Insecticide	Fumigant Action At Saturation, 24°-25°C, On Small 0.012g Larvae (% Kill 48 hrs)	Contact Dusts (1%) in Pyrophyllite On Large Larvae of 0.7g wgt. mg/cm^2	Contact Dusts (1%) in Pyrophyllite On Large Larvae of 0.7g wgt. % Kill 48 hrs	LD$_{50}$ Oral (µg/g) (Large Larvae, 0.7g wgt)
DDT	15	0.53	40	31
Lindane	35	0.58	32	31
Chlordane	96.3	0.55	2	130
Lead arsenate	—	—	—	290

(d) Vs. several species of larval lepidoptera as named: 350,1124

Insecticide	Lethal Deposit$_{50}$ (µg/cm^2) As Contact Sprays For Choristoneura fumiferana	Heliothis ononis	Agrotis orthogonia	LD$_{50}$ (µg/g) Topical* For 6th Instar Larvae Of Heliothis zea (larval wgt. 250-450 mg)	Heliothis virescens
DDT	0.3	7.0	80.0	3000*	6,500**
DDD	—	—	—	3000	17,000
Endrin	—	—	—	17***	180***
Lindane	1.9	23.0	5.5	—	—
Chlordane	140.0	non-toxic	18.0	—	—
Toxaphene®	—	—	—	2000	18,000
Malathion	—	—	—	130	160
Bayer L13/59	—	—	—	30	60
Bayer 17147	—	—	—	40	54
Shell OS-2046	—	—	—	4.8	4.8
DNOC	4.0	16	7.5	—	—
Nicotine	42.0	400	non-toxic	—	—
Pyrethrins	0.05	4.0	8.2	—	—

*Applied to abdominal dorsum, in methylethyl ketone solution. **Topical LD$_{50}$ in acetone, applied to thorax, = 73 µg/g ± 9.9, 83 µg/g ± 14.9 reared respectively on soybean and hairy vetch. ***Topical LD$_{50}$ in acetone, applied to thorax, for H. zea = 8.3 (6-12.7) µg/g; for H. virescens = 8.3 (6.5-12.2) µg/g.

(16) DDT and other substances vs. Orthoptera:

(a) Vs. *Locusta migratoria migratorioides* (young, virgin adults). Topical application in tractor vaporizing oil + cyclohexanone (9:1): 1585

Insecticide	LD_{50} 96 Hrs		LD_{95}	
	(μg/locust)	(μg/g)	(μg/locust)	(μg/g)
DDT*	140.0 ± 7.6	133.0	258.0 ± 18.6	245.0
Methyl parathion	0.94 ± 0.1	0.89	2.3 ± 0.52	2.2
Lindane	3.89 ± 0.21	3.69	12.9 ± 2.09	12.2
DNOC	10.4 ± 0.1	9.9	19.3 ± 0.897	18.3
Chlordane	20.4 ± 1.05	19.3	110.0 ± 30.9	104.0
Toxaphene*	40.2 ± 2.88	38.1	123.0 ± 16.9	116.0

*LD_{50} 120 hrs.

(b) Vs. *Melanoplus differentialis* adults:

Insecticide	Topical LD_{50} (μg/g)	Oral LD_{50} (μg/g) (On Leaves)
DDT	>3300 ; 9380	>1350; 2579; 1170 (colloidal, direct to mouth parts)
Toxaphene	61 ; 73.9	75 ; 91.5
Chlordane	9.8; 16.3	12.0; 21.8
Lindane	1.6; 3.4	6.6; 6.7
Heptachlor	1.6; 2.6	4.4; 6.0
Aldrin	1.8	2.3
Dieldrin	1.4	3.7
Parathion	0.7; 0.8	6.0; 8.9
TEPP	4.4	—
HETP	18.4	—

(17) DDT and other compounds vs. *Oncopeltus fasciatus*. Insecticides in highly purified form in acetone solution. LD values calculated from regression equations, derived from average mortalities of 3 replicates involving some 5700 adult ♀ insects: 348

Insecticide	By Injection (μg/g)				Toxicity Ratios At			
	LD_{50} 24 hrs	LD_{50} 48 hrs	LD_{95} 24 hrs	LD_{95} 48 hrs	LD_{50} 24 hrs	LD_{50} 48 hrs	LD_{95} 24 hrs	LD_{95} 48 hrs
p,p'-DDT	31.0	11.0	1043	437	1.0	1.0	1.0	1.0
Aldrin	4.5	2.5	72	43	6.9	4.6	14.5	10.2
Dieldrin	6.9	3.8	61	39	4.5	2.9	17.1	11.2

(18) DDT and other compounds vs. stored products insects. Insecticides mixed with 20 stored dry grains:

Insecticide	LC_{50} (ppm) For		
	Sitophilus granarius	*Ephestia kühniella*	*Tribolium confusum*
DDT	16	860	16
Lindane	0.1	10	3
Chlordane	1.3	36	0.2
Hexachloropropene	450	4	10

(19) DDT and other compounds. Comparative effectiveness vs. *Popillia japonica* as contact sprays: 1914

Insecticide and Formulation	Dosage (Active Ingredient Lbs/100 gals)	Time for 100% KD (hrs)	Mortality 24 hrs (%)
DDT 30% emulsion	3.0	4	100
Dilan 25% emulsion	(a) 0.25; (b)0.5	1	100
EPN® 27% wettable powder	(a) 2.0; (b) 3.0	4 (b)	100
Malathion 50% emulsion	(a) 2.0; (b) 3.0	(a) 4; (b) 1	100
Metacide 6.3% emulsion	(a) 0.125; (b) 0.0625; (c) 0.03125	(a) 1; (b) 2; (c) 4 (98%)	100
OMPA	1.0, 2.0, 3.0	at 4 only 24-31% KD	100
NPD 85% emulsion	1.0, 2.0, 3.0	at 4 only 5-21% KD	100
Systox® 32.1% emulsion	(a) 0.125; (b) 0.25; (c) 1.0	at 4 (a) 5%, (b) 97%, (c) 98% KD	100
Lindane 20% emulsion	(a) 0.25; (b) 0.125; (c) 0.0625	(a) (b) 1 hr; (c) 4	100
Methoxychlor 20% emulsion	1.0, 1.5, 2.0	0.5	100

(20) DDT and pyrethrins vs. *Chaoborus punctipennis*, larvae and pupae: 2018

Concentration (ppm)	Mortality At 48 hrs Exposure (%)			
	DDT		Pyrethrins	
	larvae	pupae	larvae	pupae
30	—	100	—	100
40	—	95	—	100
50	—	90	—	100

Concentration (ppm)	Mortality At 48 hrs Exposure (%) DDT		Pyrethrins	
	larvae	pupae	larvae	pupae
75	100	90	100	100
100	98	63	100	100
200	90	30	95	65
400	61	0	88	10
600	52	—	64	—
800	39	—	51	—

(21) DDT and other compounds vs. Pediculus humanus corporis, Cimex lectularius and lice of livestock and poultry:

(a) Contact sprays vs. Pediculus and Cimex. Solutions in P31 oil. Sprays applied at 0.36 mg/cm^2 at which rate the oil carrier is harmless. 413, 418,414

Insecticide	LC_{50} (%) For Pediculus	Cimex	LD_{50}, Contact Spray For Pediculus µg/insect	µg/g	Cimex µg/insect	µg/g
DDT*	0.3	0.56	0.054	27	0.25	63
DDD	0.9	1.2	—	—	—	—
DFDT	1.4	5.0	—	—	—	—
Methoxychlor	0.9	0.5	—	—	—	—
Lindane	0.016	0.051	0.003	1.5	0.023	6.0
p-Chlorophenyl chloromethyl sulfone	0.1	0.2	—	—	—	—
Pyrethrins	0.47	0.045	0.085	42	0.02	5.0
Pyrethrins + 2% isobutyl undecyleneamide	0.038	0.026	0.007	3.5	0.012	3.0
Lethane® 384	1.5	4.0	0.27	135	1.8	450
Lethane® Special	2.4	12.5	—	—	—	—
Thanite ®	3.2	75.0	—	—	—	—
Lauryl thiocyanate	6.0	19.5	—	—	—	—
Bis-ethyl xanthogen	6.2	75.0	—	—	—	—
Lethane® 60	8.1	32.0	—	—	—	—
Benzyl benzoate	21.0	75.0	—	—	—	—

* For Pediculus eggs DDT, at >3% (saturated solution), yielded but 8% kill. As dusts at 10, 5, 1% in kaolin, vs. Pediculus gave 100% kill of adults (in 24 hrs at 10, 5%) no kill of eggs; vs. Cimex gave 100% kill of adults at 10, 5%, 96% kill at 1%. At 0.5 and 0.25% kills of adult Pediculus were respectively 61%, 21%, of Cimex 35% at 0.5% concentration.

(b) Duration of toxicity for Cimex lectularius in sprayed beds. Heavily infested houses: 2072

Spray	Amount Applied (cc)	Time After Treatment At Which 100% Kills Were Still Given
DDT 20%, o-dichlorobenzene 40%, in kerosene	140	281 days
DDT 5%, in kerosene	195	64 "
DDT 5%, in aqueous emulsion	250	133 "
DDT 10%, cyclohexanone 5%, in kerosene	250	104 "

(c) Vs. lice of livestock and poultry. Spot treatments, dips and dusts: 2862

Insecticide	Vs. Haematopinus eurysternus* % Mortality, 24, 48 hrs, At								Effective (wks)	Vs. Bovicola caprae, Bovicola limbatus** % Mortality 24, 48 hrs At Conc.%								Infestation after 4 wks
Concentration:	.002%	.005%	.01%	.05%	.1%	.25%	.5%	1.0%		.002	.005	.01	.025	.05	.1	.2	.25	
DDT	—	—	—	—	—	100	100	—	(3,4)	—	—	—	—	—	—	—	100	0
Toxaphene®	—	—	—	—	—	—	100	—	4	—	—	—	—	—	—	—	—	—
Strobane	—	—	—	—	—	—	100	—	4	—	—	—	—	—	100	100	—	0
Endrin	—	—	—	—	—	—	—	—	—	—	—	—	—	100	—	—	—	0
Isodrin	—	—	—	—	—	—	—	—	—	—	—	—	—	100	—	—	—	0
Malathion	—	—	—	100	—	—	100	—	(1,2)	—	—	—	100	100	100	—	100	0
Parathion	—	25	100	100	—	—		—	(0,3,3)	—	—	—	—	—	—	—	—	—
Chlorthion	—	—	—	—	—	100	—	—	1	100	—	—	—	—	—	—	—	0
Dipterex®	—	—	—	—	100	100	—	—	(0,1)	100	—	100	100	100	100	—	—	light
Bayer 21/199	—	—	—	100	100	100	—	—	(1,1,2)	100	—	—	—	—	—	—	—	0
Bayer 21/200	—	—	—	—	—	—	—	—	—	25	—	—	—	—	—	—	—	light
Diazinon	5	25	95	100	100	100	—	—	(1,1,1,1,2,2)	—	100	—	100	100	—	—	—	0
Pirazinon	—	—	—	—	—	100	—	—	3	—	—	—	—	—	—	—	—	—
EPN®	25	100	100	100	—	—	—	—	(0,1,1,1)	100	—	—	—	—	—	—	—	0
NPD	—	—	—	100	—	—	—	—	1	—	—	—	—	—	—	—	—	—
2-Pivalyl indanedione				100	100	100	100	100	(2,2,2,2,3)	—	—	—	—	—	—	—	—	--

*=As spot treatments on cattle with emulsions and wettable powders. **=As dips for goats. As dusts in kaolin the following: DDT, toxaphene, strobane chlordane methoxychlor, at 5% and DDD, lindane, malathion, diazinon at 1% completely controlled on poultry original infestations of Eomenacanthus stramineus. All remained effective for 4 weeks save methoxychlor, lindane, malathion and diazinon which permit light reinfestation in 2-4 weeks.

(22) Speed of toxic action of DDT and other compounds vs. Macrosiphum pisi. Contact dusts in talc applied in the dusting tower to insects on Vicia faba plants: 520

Insecticide	Concentration (%)	°F	Time (Hours: Minutes) To Yield 50% Mortality	98% Mortality
DDT	5	72	0:57	1:45
Nicotine	1	72	0:15	1:12
"	3	72	0:12	0:50
TEPP	0.18	74	0:20	0:56
Rotenone	5	72	0:47	1:23
Lindane	1	72	0:56	1:54
Parathion	1	70	1:8	1:43
"	2	70	1:21	1:53
Methoxychlor	10	75	2:1	5:34
DDD	5	72	2:34	4:35
Aldrin	1	75	3:44	7:32
Dieldrin	1	75	4:7	6:43
EPN®	0.86	74	5:26	8:6
Chlordane	5	72	9:24	18:8
Toxaphene	5	72	13:20	19:1
Talc	100	67-72	13:28	23:51

(23) Toxicity of DDT and other compounds for adult Anasa tristis. Topical application in acetone solution: 3376

Insecticide	% Mortality At 72 hrs With Dosages Indicated (µg/g) 32	64	128	256	512
DDT	—	—	20	30	76.7
Toxaphene	—	—	16.7	66.7	82
Chlordane	—	—	36.7	80	90
Dieldrin	—	—	70	100	100
Isodrin	—	—	90	100	100
Heptachlor	—	83.3	90	100	100
EPN®	—	—	100	100	100
Endrin	—	—	100	100	100
Aldrin	—	93.3	100	100	100
Lindane	83.3	100	100	100	100
Parathion	100	100	100	100	100

(24) Toxicity of DDT employed as an aerosol. Various combinations of DDT, cyclohexanone, lube oil, dichlorodifluoromethane. Vs. Thrips tabaci and Myzus persicae in the greenhouse: 2879

DDT (g/1000 ft^3)	$Feet^3$ Treated	% Mortality Thrips tabaci adults	 larvae	 Myzus persicae
2.6	1,152	99.7	79.3	93.0
1.3	1,152	93.4	65.1	89.1
1.25	24,256	97.6	—	—
1.25	12,128	98.5	—	—
1.25	12,128	96.2	—	—
.88	1,152	78.3	12.7	47.9
.88	1,152	100	76.2	69.1
.65	1,152	74.4	40.9	77.1

(a) Found toxic under the same conditions to: Thrips nigropilosus, Hercinothrips femoralis, Trialeurodes vaporariorum, Aphis maidis, Rhophalosiphum rufomaculata, Gryllodes sigillatus, Periplaneta americana, Musca domestica, Lycoria inconstans, Armadillidium nosatum.

(25) DDT and its fluorine analogues: 2229

(a)

Drosophila melanogaster (Exposed to Residues)

($\mu g/cm^2$) (on filter paper)	% Mortality 24 hrs With DDT	DFDT
0.16	78	63
0.08	52	36
0.04	35	23
0.016	24	0

Aonidiella aurantii (Crawler Stage)(Contact Sprays)

Concentration (cc 20% xylene solution/liter)	% Mortality With DDT	DFDT
5	100	90
2	100	68
1	100	55
0.5	99	0

(b)

Toxicity and speed of action vs. Drosophila melanogaster and Heliothrips haemorrhoidalis:

(b)

Toxicity and speed of action vs. Drosophila melanogaster and Heliothrips haemorrhoidalis:

Compound	Drosophila Time (hrs) For KD_{50} On Residues: 15$\mu g/cm^2$	Heliothrips: % Mortality 24 hrs With Contact Sprays At Concentration Shown									
		1.0	0.1	0.05	.025	.01	.0075	.005	.0025	.001	.0005
DDT	8	—	—	—	—	—	—	100	88	46	25
2,2-Bis-(p-fluorophenyl)-1,1,1-trichloroethane (DFDT)	1	—	—	—	—	100	60	37	0	—	—
DDD	—	—	100	100	96	72	—	—	26	—	—
2,2-Bis-(p-fluorophenyl)-1,1-dichloroethane (DFDD)	3.5	100	—	94	90	57	—	—	—	—	—
2,2-Bis-(p-fluorophenyl)-1,1,1-trifluoroethane	5	—	52	33	—	—	—	—	—	—	—
2,2-Bis-(p-chlorophenyl)-1,1,1-trifluoroethane	6	—	34	28	—	—	—	—	—	—	—
2,2-Bis-(p-chlorophenyl)-1,1-dichloroethylene	24	24	—	—	—	—	—	—	—	—	—
2,2-Bis-(p-fluorophenyl)-1,1-dichloroethylene	6	100	0	—	—	—	—	—	—	—	—
3,3-Bis-(p-chlorophenyl)-2,1,1-trichloropropene	24	0	—	—	—	—	—	—	—	—	—
3,3-Bis-(p-fluorophenyl)-2,1,1-trichloropropene	24	31	—	—	—	—	—	—	—	—	—
4,4'-Dichlorobenzohydrol	24	10	—	—	—	—	—	—	—	—	—
4,4'-Difluorobenzohydrol	24	67	—	—	—	—	—	—	—	—	—
4,4'-Dichlorobenzophenone	24	42	0	—	—	—	—	—	—	—	—
4,4'-Difluorobenzophenone	24	—	17	—	—	—	—	—	—	—	—

Insect	Conditions	Results
Listroderes obliquus (adult)	On leaves dusted with 5% dusts (0.085 mg/cm^2)	96 hrs kill: DDT-70%; DFDT-100%.
Apantesis proxima (larva)	10% toxicants in baits 0.1g/larva	96 hrs kill: DDT-65%; DFDT-30%.
Phryganidia californica (larva)	Leaves dusted with 5% dusts (0.085 mg/cm^2)	96 hrs kill: DDT-75%; DFDT-55%.
Tribolium confusum (adult)	Residues at 15 $\mu g/cm^2$	120 hrs kill: DDT-81%; DFDT-91%; DDD-2%; DFDD-2%.
Cantharis consors (adult)	Residues at 150 $\mu g/cm^2$	KD: DDT-100% (24 hrs); DFDT-100% (1.5 hrs); DDD-80% (24 hrs). DFDD-100% (24 hrs).
Lucilia sericata (adult)	Residues 1 mg/cm^2	KD: DDT-100% (24 hrs); DFDT-100% (2 hrs)
Apis mellifera (adult)	Residues 1 mg/cm^2	% Kill: DDT-100% (20 hrs); DFDT-100% (5 hrs).
Pogonomyrmex barbatus	Residues 1 mg/cm^2	KD: DDT-100% (48 hrs); DFDT-100% (16 hrs).
Heliothrips haemorrhoidalis	Exposed on oranges dipped in 0.1% solutions	Initial mortality: 100%-DDT, DFDT; 14 day old residues: DDT-95% kills; 1 day old residues DFDT-32% kill; 4 day old residues DFDT-17% kill.

(26) DDT and other compounds vs. DDT-R and DDT-nonR biotypes of Musca domestica

(a) Topical application by the measured drop method to adult insects. 78

Biotype	LD_{50} 24 hrs (μg/fly)						
	DDT	DDD	Methoxychlor	Toxaphene	Lindane	Heptachlor	Pyrethrins
Bellflower (DDT-R)	10	20	1	0.6	0.08	0.06	1
San José (DDT-R)	0.7	—	0.3	0.4	0.05	0.07	2
Ontario (DDT-R)	0.5	—	0.3	0.5	0.05	0.07	2
Riverside (DDT-R)	0.5	—	0.3	0.5	0.06	0.07	2
Laboratory (DDT-nonR)	0.02	0.1	0.07	0.2	0.01	0.03	1

(b) Exposure to residues: 78

Insecticide	Residue (mg/ft^2)	Time (Minutes) To Yield 50% and 100% "Knockdown"					
		Bellflower		San Jose'		Laboratory	
		KD_{50}	KD_{100}	KD_{50}	KD_{100}	KD_{50}	KD_{100}
DDT	100	720	2880	420	1440	91	152
Methoxychlor	100	255	360	56	108	37	67
Lindane	10	11	15	16	20	13	20
Heptachlor	10	40	52	48	60	44	51

(c) Exposure to residues and to direct application of DDT and other compounds. 1803,3320

Insecticide	Residue Exposure							Topical LD_{50} (μg/fly) adult ♀♀		
	Lethal $Time_{70}$ (min)			Lethal $Time_{50}$ (min)						
	Orlando Special ♀	Bell-flower ♀	Labora-tory ♀	Orlando #1	LDD	Ballard	Labora-tory	Orlando Special	Bell-flower	Labora-tory
DDT	230	184	3.2	ca1440	>240	344	9	12.3	8.3	0.12
Methoxychlor	150	33	—	—	—	—	—	2.4	2.7	0.34
BHC 95% γ	—	—	—	—	—	—	—	0.044	0.058	0.015
BHC 12% γ	56	44	—	—	—	—	—	—	—	—
Lindane	—	—	—	16.4	65.6	229.3	10.9	—	—	—
Dieldrin	—	—	—	9.1	>120	—	<1	0.024	0.014	0.012
Chlordane	—	—	—	—	—	—	—	0.2	0.11	0.062
Heptachlor	—	—	—	—	—	—	—	0.031	0.020	0.017
Pyrethrins	—	—	—	—	—	—	—	0.955	0.955	0.48
Pyrethrins + piperonyl butoxide 1:10	—	—	—	—	—	—	—	0.082	0.085	0.048

d) Residual toxicity of DDT:

(1) The persistence of DDT applied to surfaces, with long retention of toxicity for insects coming in 2765
contact with such surfaces, has remained one of the most remarked upon insecticidal properties of 266
DDT. Among the factors of importance in exploiting this property of DDT is the nature of the surface 268
to which it is applied. Studies of the penetration of DDT into wood surfaces and as an ingredient of 267
paints and other surface coatings, may be found in the references given opposite.

(2) Time required for complete "knockdown" of Musca domestica (adults), exposed in unpainted wooden 2010
cages sprayed with 5% solutions of DDT in various solvents, and on residues of various ages.

Days Between Treatment Of Cage and Exposure of Insects; (age of residue) (days)	Minutes Elapsing Before KD_{100} of Flies Exposed To Cages Treated With DDT (5%) In						
	Ethylene dichloride	Dibutyl phthalate	Ethylene dichloride (emuls.)	Dibutyl phthalate (emuls)	Kerosene	Benzyl benzoate + kerosene	Benzyl benzoate + kerosene (emuls)
15	30	20	32	41	15	23	17
20	58	63	44	115	29	29	28
26	59	115	56	222	37	46	33
33	73	172	47	280	60	57	57
45	58	382	55	384	92	102	53
53	48	390	54	390	122	116	64
60	67	259	92	245	92	112	76
67	108	262	101	453	166	128	23
75	82	202	50	230	70	91	72
80	81	403	142	428	87	80	84
86	156	321	275	420	156	94	106
93	301	326	297	422	300	233	316
100	—	—	—	—	222	319	344
115	314	—	—	356	438	402	450
265	80	—	—	125	103	97	109

(3) % Mortality in 24 hours of adult ♀ Anopheles quadrimaculatus, exposed for 60 minutes to deposits of DDT at 200 mg/ft^2 from DDT-xylene emulsions. Various surfaces: 974

Surface	Age of Residue In Weeks											
	5	9	15	23	25	27	29	31	33	35	37	39
	% Mortality (24 hrs) after 60 minute exposure											
Pine plywood	93	89	91	94	91	69	69	60	54	64	71	72
Dry bamboo	96	93	100	98	90	85	92	96	88	86	88	88
Rusty metal screen	99	98	99	99	93	84	85	92	85	78	83	91
Rusty sheet metal	98	92	81	79	85	86	90	92	81	76	83	90
Bark	—	90	86	88		87	—	—	—	—	—	—
New sheet metal	84	79	64	51	54	67	71	69	69	57	62	58
Glass	77	77	77	75	71	74	60	58	48	53	68	73
Tile	78	72	77	89	84	70	69	64	50	58	70	53
Palmetto thatch	—	71	82	75	—	74	—	—	—	—	—	—
New metal screen	98	90	79	65	46	30	37	51	42	38	42	36
Plexiglass	50	56	70	70	59	59	59	57	36	34	42	44
Shellacked wood	—	74	70	40	23	21	39	—	—	—	—	—
Synthetic fabrics	68	48	44	58		58	50	46	45	37	33	38
Cement	55	37	35	44	31	16	10	—	—	—	—	—
Waxed wood	—	21	37	19	—	—	—	—	—	—	—	—

e) Effects of DDT on beneficial insects:

(1) DDT and honeybees: (Also consult the section in this work titled Bees and Insecticides.)

(a) Reports on the hazard of DDT for honeybees are conflicting. DDT may be considered of questionable 3099
safety to honeybees on flowering plants. Toxicity is influenced by particle size. Contact toxicity, in 3247
the temperature range 20°-36°C, ranges from 32 to 560 μg/bee.

(b) 110g pollen paste containing 0.25g DDT fed to a hive of Apis mellifera had no injurious effects. The 3247
LD_{50}, oral, for adult worker bees = 4.6 μg/bee. 908

(c) Dusting inside of hives of Apis indica with DDT dusts of less than 5% DDT content produced no injurious effects; 10% dusts yielded complete mortality. 3247

(d) 0.25 ounce honey with 0.05% DDT fed daily to hive of Apis indica yielded 96.5% mortality after 7 days.

(e) DDT concentrations in commercial contact sprays required to yield 20, 50, 95% kills by contact poisoning as g/100cc DDT in dispersible powder formulation (Guesarol E) are respectively: 0.1, 0.16, 0.39g, for Apis mellifera.

(f) On apple, Cineraria and Michaelmas Daisy flowers, sprayed 1 day before exposure of bees with 1%, 0.5%, 0.2% DDT as Guesarol E: On apple at 1%: 0% mortality; on Michaelmas daisy: 4%; on Cineraria at 0.5%: 0% mortality; on daisy: 4%; at 0.2% on Cineraria: 0% mortality. With 5% dusts on apple blooms bees, exposed 1 day after treatment, gave 0% mortality. 3247

(g) Effect of DDT (as Guesarol E spray) films on glass cage walls. Adult Apis mellifera workers: 3247

% DDT	% Mortality On	
	1st Day	Fifth Day
1	100	—
0.5	93	100
0.2	37	67
0.1	13	37
Control	5	15

(h) Amount of DDT and other compounds required as stomach poisons to yield various degrees of mortality on the 3rd day. Insecticides in pure form: suspended in diluted honey medium: 3247

Toxicant	Dosage (mg x 10^{-3}/bee) To Give Kills of		
	20%	50%	95%
DDT	5.4	9.1	25
Lindane	0.03	0.08	0.54
Lead arsenate	32	86	610
" " (on fifth day)	6.1	20	210

(i) Apis mellifera, caught and caged after successive visits over three days to fields in open blossom treated with DDT, showed no mortality attributable to DDT during the ensuing 6 days. (Bees may be killed by 1 minute contact with open blooms in BHC treated fields.) 3247

(j) DDT is reported non-toxic in field concentrations for Bombus pratorum, Andrena spp. Susceptibility of Bombus terrestris and B. agrorum workers is comparable. Osmia rufa was not affected by short contact with DDT treated flowers. Queens and drones of Bombus terrestris and B. agrorum are particularly DDT resistant. This is important since in Spring, at time of fruit blossom spraying, the Bombus "population" is represented almost wholly by queens. 3247

(2) Vs. beneficial insects other than bees:

(a) DDT is toxic to at least a moderate degree to such beneficial genera as Orius, Geocoris, Nabis, Chrysopa, Hippodamia. 3171

(b) Laboratory tests. Adult insects placed on plants previously dusted by the vacuum dusting method: 1404

Insecticide And Conc. in Dust	% Mortality 24 hrs. Of		
	Collops vittatus	Hippodamia convergens	Coleomegilla maculata
DDT (5%)	38	6	32
Perthane (5%)	23	6	12
Strobane (5%)	10	18	12
Heptachlor (2.5%)	41	30	38
Toxaphene (10%)	32	12	36
Endrin (1%)	27	10	18
Dieldrin (2%)	36	4	24
Parathion (2%)	65	78	98
Malathion (5%)	47	90	100
Chlorthion (5%)	64	82	100
Diazinon (4%)	37	66	100
Control	11	4	0
Lowest Significant Difference (5% level)	20	24	26

(3) Dacus dorsalis and its internal parasite Opius öophilus were both highly resistant to DDT in soil and topical treatments. 3048

(4) DDT apparently does not favor, by destruction of parasites or predators, upsurges in Aonidiella aurantii or A. citrina. 734

(5) DDT is reported to produce from 50%-95% mortality or complete elimination of the following beneficial predaceous arthropods: 2650

Leptothrips mali
Scolothrips sexmaculatus
Haplothrips faurei
Hyaliodes hartii
Diaphnidia pellucida
Deraeocoris fasciolus
Plagiognathus obscurus
Criocoris saliens
Pilophorus perplexus
Campylomma verbasci
Cyrtorhinus mundulus
Anthocoris musculus
Anthocoris nemorum
Orius tristicolor
Nabis ferus
Geocoris punctipes

Stethorus punctum
Stethorus pictipes
Stethorus punctillum
Scymnus binaevatus
Rodolia cardinalis
Coccinella septempunctata
Adalia bipunctata
Coleomegilla maculata
Hippodamia convergens
Chrysopa sp.
Conwentzia sp.
Syrphus sp.
Typhlodromus spp.
Anystis agilis
Hemisarcoptes malus
Biscirus australicus

Allotropa sp
Aphelinus mali
Aphytis mytilaspidis
Clausenia purpurea
Dacnusa gracilis
Diaeretus rapae
Encarsia formosa
Macrocentrus ancylovorus
Metaphycus luteolus
Opius sp.
Pachysema sp.
Prospattella aurantii
Pseudaphycus sp.
Pseudhomalpoda prima
Tetracnemus pretiosus
Trichogramma minutum

(6) After application of DDT, resurgences have been noted in "populations" of the following harmful arthropods: 2650

Tetranychus telarius
Tetranychus mcdanieli
Tetranychus schoenei
Tetranychus pacificus
Metatetranychus citri

Coccus hesperidum
Icerya purchasi
Planococcus citri
Pseudococcus adonidum
Pseudococcus maritimus

Aphis gossypii
Aphis spiraecola
Phylloxera vitifoliae
Brevicoryne brassicae
Chromaphis juglandicola

Metatetranychus ulmi
Oligonychus ununguis
Oligonychus yothersi
Bryobia praetiosa
Eurytetranychus buxi
Vasates lycopersicae
Phyllocoptruta oleivora
Smynthurus viridis
Eulia velutinana
Lyriomyza sp.

Chrysomphalus ficus
Eulecanium corni
Eulecanium pruinosum
Aonidiella aurantii
Aonidiella citrina
Aonidiella orientalis
Lepidosaphes beckii
Aphis fabae
Spilonota ocellana

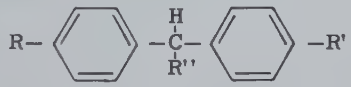
Macrosiphum solanifolii
Capitophorus fragaefolii
Eriosoma lanigerum
Bremisia tabaci
Earias insulana
Diparopsis watersi
Heliothis armigera
Tortrix postvittana
Rhagoletis pomonella

f) Structure and toxicity: [Refs.: 2472,2262,2127,2937,767,2844,2240,260,2642,1933,2641,2644,2040,353,2231,367, 2551,415,2975,3203,767,2337,2230,2317,819,2890,2129,194,1325,2845,2096,1816,366, 2502,2234,642;1818,2094,261,2229,1300,2690,648,362,2828,2543,1666,212]

(1) DDT and related compounds have been studied extensively to uncover the relationship of chemical structure, toxicity, and mode of action. Several substances closely related to DDT have been found to have great advantages as insecticides and some among them have shown exceptional specificity of action toward particular insect genera and species. In view of the last statement, generalization is hazardous, but always allowing for the possibility that any analogue or structural relative of DDT may be as toxic, or indeed more toxic, than DDT for one or more species, in general modifications of structure have led to diminution of activity. However, it must be remembered that while DDT itself is generally ineffective for phytophagous acarines, modifications of the structure have led to compounds intensely toxic for these forms.

(2) Two tabulations follow which serve to give a comparative view of the toxicity for certain insects of DDT and its structural analogues and relatives.

(a) Comparative toxicity of DDT analogues. Modified from 2231.



R	R'	R''	Pediculus humanus LC$_{50}$ (%)	Cimex lectularius LC$_{50}$ (%)	Macrosiphoniella sanborni LC$_{50}$ (relative)	Oryzaephilus surinamensis LC$_{50}$ (relative)	Anopheles quadrimaculatus LC$_{50}$ (ppm)	Heliothrips haemorrhoidalis LC$_{50}$ (%)	Musca domestica LD$_{50}$ (μg/g)
Cl	Cl	CCl_3 (DDT)	0.3	0.53	1.0 (standard)	1.0	0.002	0.001	1.65
F	F	CCl_3 (DFDT)	1.4	5.0	1.01	4.4	0.007	0.006	5.0
Br	Br	CCl_3	0.6	1.4	1.6	1.1	0.0025	0.06	1.95
I	I	CCl_3	—	—	trace	trace	—	—	—
CH_3	CH_3	CCl_3 (Methyl-DDT)	1.7	3.6	—	—	0.007	0.03	9.0
C_2H_5	C_2H_5	CCl_3 (Ethyl-DDT)	5.0	4.0	—	—	—	0.04	5.5
CH_3O	CH_3O	CCl_3 (Methoxychlor)	0.9	0.55	4.0	2.6	0.01	0.03	3.4
C_2H_5O	C_2H_5O	CCl_3	1.8	0.8	0.83	1.4	—	—	—
H	H	CCl_3	7.5	12.0	16	—	1.0	1.0	—
OH	OH	CCl_3	0	0	0	0	>10	>1.0	—
NO_2	NO_2	CCl_3	—	—	—	—	—	>1.0	—
Cl	H	CCl_3	2.1	4.5	1.94	25	0.025	0.25	—
Cl	Cl	$CHCl_2$ (DDD)	0.9	1.2	4.35	3.12	0.001	0.006	6.5
Cl	Cl	CH_2Cl	—	—	—	—	0.06	—	—
Cl	Cl	CCH_3	8.5	>20	16	200	—	1.0	—
Cl	Cl	CBr_3	—	—	3.3	10.3	0.1	—	—
Cl	Cl	$CHNO_2CH_3$	—	—	—	—	—	—	4.75

(3) Toxicity of DDT analogues: Relation of chemical structure and toxicity: 415

(a) Tests with adult Pediculus humanus and Cimex lectularius, by direct spray in cases where oil or water solubility of the analogue in question permitted, otherwise by dusts:

(1) Sprays made in refined white oil, P31, volume constant, concentration varied; sprayed to give average deposit of 0.36 mg/cm^2.

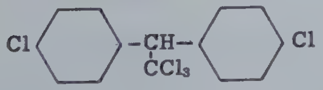
(2) Dusts applied as the compound neat or in kaolin dilution.

(3) In spray tests: The insects were sprayed directly while resting on absorbent paper. In dust tests: Bed bugs were shaken in the powders; lice were allowed to rest in contact with dust impregnated cloth.

(4) LC$_{50}$ (%) estimated from log conc./probit graphs. Louse mortality determined at 3 days; bed bug mortality at 7 days.

(5) Aëdes aegypti was tested by spray cabinet method of David.

(b)

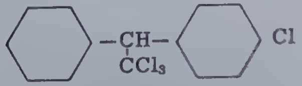


p,p'-DDT: m.p. 108°C, sol in P31 oil ca 2%

LC$_{50}$ (%)	
Cimex	Pediculus
0.53	0.3

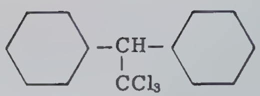
Aëdes 32% Kill at 0.4%

(1) Alteration in number and position of chlorine atoms: Elimination of Cl from benzene rings.



Cimex	Pediculus
4.5	2.1

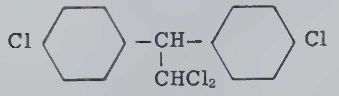
Phenyl-chlorophenyl-trichloroethane m.p. 73°C, sol P31 oil ca 4%



Cimex	Pediculus
>12	7.5

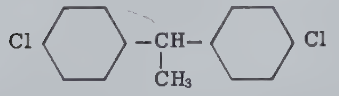
Diphenyl-trichloroethane m.p. 62°C, sol P31 oil ca 12%

(2) Displacement of chlorine from the ethane nucleus:



Cimex	Pediculus
1.2	0.9

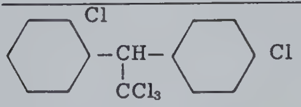
Dichlor-diphenyl-dichlorethane m.p. 111°C, sol P31 ca 2% Aëdes 35% Kill At 1.0%



Cimex	Pediculus
>20	8.5

Dichlor-diphenylethane m.p. 56°C, sol P31 24%

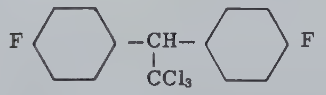
(3) Position of chlorines on benzene rings:



Cimex	Pediculus
≫14	5.5

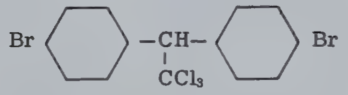
iso-DDT, o,p-DDT m.p. 73°C, sol P31 ca 12% Aëdes 32% Kill At 5.0%

(4) Substitution of other halogens for the para-Cl atoms:



Cimex	Pediculus
5	1.4

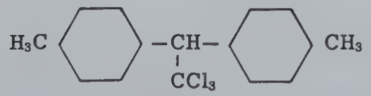
DFDT m.p. 45°C, sol P31 ca 4%



Cimex	Pediculus
1.4	0.6

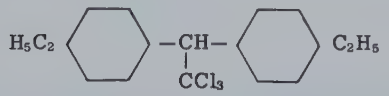
"Bromine-DDT" m.p. 142°C sol P31 ca 2%

(5) Substitution of alkyl groups for para-Cl atoms: 415



LC$_{50}$ (%)	
Cimex	Pediculus
3.6	1.7

Dimethyl-diphenyl-trichloroethane m.p. 90°C, sol P31 ca 8%



Cimex	Pediculus
4.0	5.0

Diethyl-diphenyl-trichloroethane, liquid, miscible

(c) Substitution of alkoxy-groups for para-Cl atoms:

(1) Aliphatic series

	LC$_{50}$ (%)		Conc & % Kill
Group substituted for both para-Cl's	Cimex	Pediculus	Aëdes
methoxy, CH_3O- m.p. 88°C, sol P31 ca 2%	0.55	0.9	54% Kill At 1.0%
ethoxy, C_2H_5O- m.p. 107°C, sol P31 ca 2%	0.8	1.8	
propoxy, n-C_3H_7O- m.p. 62°C, sol P31 ca 8%	2	6	
butoxy, n-C_4H_9O- m.p. 50°C, sol P31 ca 12%	>8	>8	
amoxy, n-$C_5H_{11}O-$ m.p. 66, sol P31 ca 8%	>8	>8	

(2) Other compounds with ether linkages in parapositions:

		% Kill undiluted dusts
cetoxy, $C_{16}H_{31}O-$ m.p. 78°C, sol P31 ca $\frac{1}{2}$%	0	4
allyloxy, $CH_2=CH-CH_2O-$ m.p. 81°C, sol P31 ca 2%	24	65
benzyloxy, $C_6H_5CH_2O-$ m.p. 139°C, sol P31 ca $\frac{1}{4}$%	0	0
acetoxy, CH_3COO- m.p. 140°C, sol P31 ca $\frac{1}{4}$%	0	3
benzoyloxy, C_6H_5COO- m.p. 234°C, sol P31 ca $\frac{1}{4}$%	24	0
cinnamoyloxy, $C_6H_5CH=CHCOO-$ m.p. 158°C	5	11
dinitrophenoxy, $C_6H_4(NO_2)_2O-$ m.p. 194°C	4	0

(d) Tetra-substituted compounds:

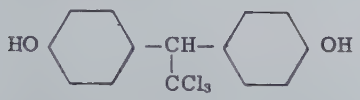
bis(2,4-methylphenyl) trichloroethane	4% Kill	13% Kill	sprayed with 5% sol m.p. 81°C sol P31 ca 4%
	% Kill in dust		
bis(3-nitro-4-chlorphenyl) trichloroethane	—	0	m.p. 47°C sol P31 ca $\frac{1}{4}$%
bis(2-chlor-5-methylphenyl) trichloroethane	—	10	m.p. 155°C sol P31 ca $\frac{1}{2}$%
bis(2-methyl-4-chlorphenyl) trichloroethane	—	0	m.p. 106°C sol P31 ca 1%
bis(3,4-dimethoxyphenyl) trichloroethane	0	12	m.p. 115°C sol P31 ca $\frac{1}{4}$%
bis(2,5-dimethoxyphenyl) trichloroethane	10	17	m.p. 120°C sol P31 ca $\frac{1}{4}$%
bis(3-brom-4-methoxyphenyl) trichloroethane	12	8	m.p. 141°C sol P31 ca 1%

(e) Naphthalene condensates:

		% Kill undiluted dusts	
bis-naphthyl-trichloroethane	—	0	m.p. 158°C sol P31 ca $\frac{1}{2}$%
bis(5?-chlornaphthyl) trichloroethane	—	10	m.p. 223°C sol P31 ca $\frac{1}{4}$%
bis(5?-bromnaphthyl) trichloroethane	—	0	m.p. 218°C sol P31 ca $\frac{1}{4}$%

(f) Water soluble analogues: Pediculus tested by simple dipping in 10% solution 20 minute immersion, showed no appreciable mortality.

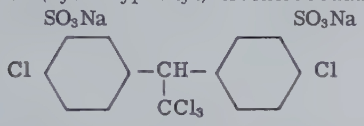
(1) Dust Tests:



415

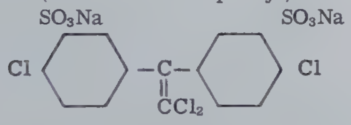
% Kill With Undiluted Dusts	
Cimex	Pediculus
0	0

bis(hydroxyphenyl)-trichloroethane m.p. 206°C



Cimex	Pediculus
10	0

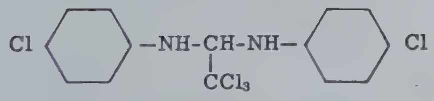
bis(4-chlor-3-sulfaphenyl)-trichloroethane, diNa m.p. 210°C



Cimex	Pediculus
0	8

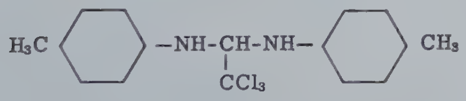
bis(4-chloro-3-sulfaphenyl)-dichlorethylene, diNa m.p. 210°C

(g) Compounds with intercalated amine groups:



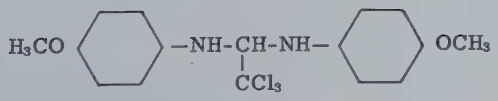
% Kill undiluted dusts	
Cimex	Pediculus
—	91

di-p-chloraniline trichloroethane m.p. 180°C



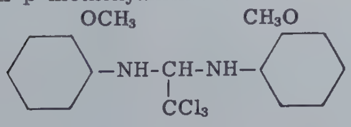
—	13

di-p-methylaniline-trichloroethane m.p. 105°C



—	37

di-p-methoxyaniline-trichloroethane m.p. 114°C



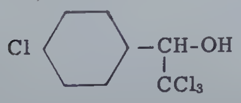
—	25

di-o-methoxyaniline-trichloroethane m.p. 114°C

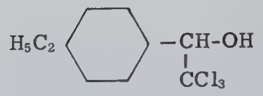
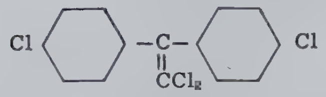
(h) Other analogues:

(1) "Half-condensation" product

LC$_{50}$ (%)	
Cimex	Pediculus
10	6.5



chlorphenyl-hydroxy-trichloroethane liquid, miscible

	LC$_{50}$ (%)	
	Cimex	Pediculus
 ethylphenyl-hydroxy-trichloroethane liquid, miscible	7.0	7.0
(2) "Dehydrochlorinated DDT"  dichlor-diphenyl-dichlorethylene m.p. 89°C, sol P31 8%	>10	>10

(c) Toxicity of pure DDT and compounds related to DDT for Anopheles quadrimaculatus 4th instar. Beaker tests; 20 larvae in each trial. At dosages of 0.1 ppm or less: 767

	Exp. Hrs.	% Mortality At						
		.0025 ppm	.005 ppm	.01 ppm	.02 ppm	.025 ppm	.05 ppm	.1 ppm
p,p' DDT	24	22-55	60-83	100	—	—	—	—
	48	80-82	93-97	100	—	—	—	—
1-Trichloro-2-(p-chlorophenyl)-2-(o-chlorophenyl) ethane	24	—	—	35	—	100	100	100
	48	—	—	45	—	—	—	—
1-Trichloro-2-(p-chlorophenyl)-2-(m-chlorophenyl) ethane	24	5	20	30	73	—	—	—
	48	22	55	77	98	—	100	100
1-Trichloro-2-phenyl-2-(p-chlorophenyl) ethane	24	—	10	15	—	60	100	95
	48	—	10	85	—	95		95
1,1-Dichloro-2,2-bis(p-chlorophenyl) ethane	24	58	88	100	—	100	100	100
	48	95	100	—	—	—	—	—
1-Chloro-2,2-bis(p-chlorophenyl) ethane	24	—	—	—	—	—	5	55
	48	—	—	—	—	—	40	100
1,1-Dichloro-2-(p-chlorophenyl)-2-(o-chlorophenyl) ethane	24	—	—	20	—	60	95	100
	48	—	—	20	—	85	100	—
1,1,1,2-Tetrachloro-2,2-bis(p-chlorophenyl) ethane	24	—	—	—	—	—	0	40
	48	—	—	—	—	—	20	95
1-Trichloro-2,2-bis(p-bromophenyl) ethane	24	60	95	95	—	100	100	100
	48	95	100	100	—	—	—	—
1-Tribromo-2,2-bis(p-chlorophenyl) ethane	24	—	—	—	—	0	5	45
	48	—	—	—	—	10	60	100
1-Trichloro-2,2-bis(p-fluorophenyl) ethane	24	—	5	85	—	100	100	100
	48	—	10	85	—	—	—	—
1-Trichloro-2,2-bis(3,5-dichloro-2-hydroxyphenyl) ethane	24	—	5	85	—	100	100	100
	48	—	10	85	—	—	—	—
1-Trichloro-2,2-bis(p-methoxyphenyl) ethane	24	—	5	50	—	55	100	75
	48	—	20	100	—	95		90
1-Trichloro-2,2-di-p-tolylethane	24	—	5	50	—	55	100	100
	48		20	100	—	95	—	—
p,p'-Dichlorodiphenyl sulfide	24	—	—	—	—	—	—	70
	48	—	—	—	—	—	—	70

Lowest concentration in which certain DDT-related compounds were found toxic to Anopheles quadrimaculatus 4th instar: 767

(1) Two or more benzene rings, halogen on ring and aliphatic carbon:

Compound	ppm
1-Trichloro-2-(p-chlorophenyl)-2-(o-chlorophenyl) ethane	0.025
1-Trichloro-2-(p-chlorophenyl)-2-(m-chlorophenyl) ethane	0.005
1-Trichloro-2-phenyl-2-(p-chlorophenyl) ethane	0.01
1,1-Dichloro-2,2-bis(p-chlorophenyl) ethane	0.0025
1-Chloro-2,2-bis(p-chlorophenyl) ethane	0.1
1,1-Dichloro-2-(p-chlorophenyl)-2-(o-chlorophenyl) ethane	0.025
1,1,1,2-Tetrachloro-2,2-bis(p-chlorophenyl) ethane	0.1
1-Trichloro-2,2-bis(p-bromophenyl) ethane	0.0025
1-Tribromo-2,2-bis(p-chlorophenyl) ethane	0.05
1-Tribromo-2,2-bis(p-bromophenyl) ethane	10 (insoluble in acetone)
1-Trichloro-2,2-bis(p-fluorophenyl) ethane	0.01
1,1-Dibromo-2,2-bis(p-chlorophenyl) ethane	10
1,1-Dibromo-2,2-bis(p-bromophenyl) ethane	10
1,1-Dichloro-2,2-bis(p-chlorophenyl) ethylene	1.0
1,1-Dichloro-2,2-bis(p-bromophenyl) ethylene	10
1-Trichloro-2,2-bis(5-chloro-2-hydroxyphenyl) ethane	>10
1-Trichloro-2,2-bis(3,5-dichloro-2-hydroxyphenyl) ethane	0.025

Compound	ppm	
1-Trichloro-2,2-bis(5-chloro-2-methoxyphenyl) ethane	>10	
1-Trichloro-2,2-bis(3,5-dichloro-2-methoxyphenyl) ethane	>10	
1-Trichloro-2,2-bis(3,5-dichloro-4-methoxyphenyl) ethane	10	
Dinitro-1-trichloro-2,2-bis(p-chlorophenyl) ethane	>10	
1-Trichloro-2,2-bis(4-chloro-3,5-dinitrophenyl) ethane	>10	
Chlorobis(p-chlorophenyl) methane	>10	
Bromobis (p-chlorophenyl) methane	10	
p-Chlorophenyl phenyl dichloromethane	10	
1-Trichloro-2,2-dichloro-3,3-dichloro-4,4-bis(p-chlorophenyl) butane	10	
2,2,3,3-Tetrachloro-1,1,4,4-tetrakis(p-chlorophenyl) butane	>10	
(2) Two benzene rings, halogen on aliphatic carbon only:		
1-Trichloro-2,2-diphenyl ethane	1.0	
1-Trichloro-2-phenyl-2-biphenyl ethane	>10	
1,1-Dichloro-2,2-diphenyl ethylene	10	
1-Trichloro-2,2-bis(p-hydroxyphenyl) ethane	>10	
1-Trichloro-2,2-bis(p-methoxyphenyl) ethane	0.01	
1-Trichloro-2,2-bis(2,5-dimethoxyphenyl) ethane	>10	
1-Trichloro-2,2-bis(3,4-dimethoxyphenyl) ethane	>10	
1-Trichloro-2,2-di-p-tolylethane	0.01	
1-Trichloro-2,2-bis-(p-tert.-butylphenyl) ethane	>10	
1-Trichloro-2,2-bis-(p-acetoxyphenyl) ethane	10	
1-Trichloro-2-(p-nitrophenyl)-2-(m-nitrophenyl) ethane	>10	
Dinitro-1-trichloro-2,2-di-p-tolylethane	>10	767
(3) Two or more benzene rings, halogen on ring only:		
Bis-(p-chlorophenyl) methane	1.0	
o,p'-Dichlorodiphenyl methane	1.0	
Bis(p-bromophenyl) methane	1.0	
Bis(p-chlorophenyl) methanol	10	
1,1,2,2-Tetrakis (p-chlorophenyl) ethylene	>10	
Bis(5-chloro-2-hydroxyphenyl) methane	10	
Bis(3,5-dichloro-2-hydroxyphenyl) methane	10	
Bis(2,4,6-trichloro-3-hydroxyphenyl) methane	>10	
1,1-Bis(5-chloro-2-hydroxyphenyl) ethane	10	
Bis(p-chlorophenyl) acetic acid	10	
Bis(p-chlorophenyl) acetamide	>10	
Bis(p-chlorophenyl) methyl methyl ether	10	
p-Chlorobenzophenone	10	
p,p'-Dichlorobenzophenone	10	
(4) One benzene ring, aliphatic CCl_3 group.		
α-Trichlorotoluene	>10	
α,α,α-2-Tetrachlorotoluene	10	
α,α,α-3-Tetrachlorotoluene	1.0	
α,α,α-4-Tetrachlorotoluene	>10	
α,α,α-3,4-Pentachlorotoluene	>10	
α,α,α-2,4-Pentachlorotoluene	10	
α,α'-Hexachloro-o-xylene	10	
α,α'-Hexachloro-m-xylene	10	
α,α'-Hexachloro-p-xylene	10	
α,α',α''-Nonachloromesitylene	>10	
1-p-Chlorophenyl-2-trichloroethanol-1	>10	
1-Phenyl-2-trichloroethanol-1	>10	
1-o-Chlorophenyl-2-trichloroethanol-1	10	
(5) Analagous structure, no halogen:		
1,1-Diphenylethane	10	
1,1-Diphenylethylene	10	
Diphenylmethane	10	
(6) Related sulfur compounds		
p,p'-Dichlorodiphenyl sulfide	0.1	
p,p'-Dichlorodiphenyl sulfoxide	10	
p,p'-Dichlorodiphenyl sulfone	1.0	
1-o-Chlorophenyl-2-trichloroethyl-p-chlorobenzene sulfonate	>10	

6) Pharmacological, pharmacodynamic, physiological, etc., insects:

a) The mode of action of DDT is imperfectly understood. 353,2231,151,1755

(1) Characteristic tremors indicate fundamental nerve tissue disturbances. 151

(2) Sensory nerves reported most sensitive, nerve ganglia least sensitive. 151

(3) Sensory impulses in abnormal bursts, with consequent spasmodic tremors, mediated by motor nerves. 151

(4) Disruption of sensory impulse coordination, with consequent behavioral abnormalities in movement, gait, equilibrium. 151

b) Particle size, shape and contact toxicity: 2194,2195,2196,2197

(1) Within range of crystal sizes to ca. 400 μ, short term contact toxicity increased with needle length; (breadth of crystal less important) in dipping tests with Tribolium castaneum.

(2) Suspensions of needle-shaped crystals were equitoxic with suspensions of much larger plate-shaped crystals at same w/v concentration.

(3) Colloidal DDT, in short term contact toxicity tests (dipping) proved less toxic than any crystal suspension.

DDT	LC_{50}, Tribolium castaneum
400 μ needles	1.0 (standard)
120 " "	2.1
240 x 140 μ plate aggregates	2.6
40 μ needles	3.9
60 x 15 μ plates	5.1
Colloidal	17.0

(4) Temperature coefficients of crystal and colloidal suspensions differ in contact toxicity tests. At 12°-30°C colloidal DDT showed a largely negative coefficient; coefficient for crystal suspensions (400 μ or less) was small to negligible.

(5) By injection (Oncopeltus fasciatus), crystal and colloidal suspensions showed equal toxicity at 27°C, as measured during 2 post-treatment days. In cool insects (10°C) colloidal suspensions were more rapid acting than crystal suspensions, but the ultimate mortality in 10 days of observation at cool storage is equalized, the equalization taking place more rapidly (2 days) in case of DFDT.

I) Entry of DDT to insect body:

a) Via the insect cuticle (as in contact toxicity, residue action) absorption by, and penetration into, insect is highly efficient. Penetration is particularly effective in regions of thin, flexible cuticle. 846,3095,3270, 3345,1008,1975

b) Via the gastro-intestinal surface: DDT is an effective stomach poison for many insects. At 1% in sugar, molasses baits DDT gave in 30 minutes 30%, in 1 hour 44%, in 24 hrs. 98% kills of Musca. 1915,353,2231, 2974,3236,3270, 2975

(1) Via either route wide variations occurred in susceptibility among different species of insects; some, susceptible to intraparenteral DDT, resist it by contact, and in some, gut wall penetration is very slight.

(2) In Musca the locus of application is reported to influence penetration rate, distribution, and accumulation at site of action. Area of contact was directly related to rate of penetration into the haemolymph and distribution over body. Distribution, from site of application, continues at a reduced rate in dead flies. Rate of absorption is generally correlated with susceptibility of an insect species and is a direct function of temperature. 2972 3189 2975 1975

(3) Topical application of C^{14} labelled DDT and DDE, yields rapid absorption and wide internal distribution via haemolymph (although haemolymph does not accumulate DDT). In Periplaneta americana, ca. 75% of applied DDT is excreted as metabolite(s) in the feces over a 24 day period. With 40 μg/insect applied, ca. 50% is absorbed in 24 hours, >95% after 6 days, with foregut, hindgut, fat body, Malpighian tubules, containing most of radioactivity. 2675 1975

(4) Dosage to kill one Musca domestica with topical application of 2 μg/fly: 1974

Site of Application	Time of Amputation	Site of Amputation	% Mortality 24 hrs	% Radioactivity Recovered In Amputated Part
Tibio-femoral joint	30 minutes later	At coxal joint	40	91
Tibio-femoral joint	4 hours later	At coxal joint	82	80
Labellum	30 minutes later	Whole labellum	84	90-93% in proboscis

Absorption and distribution of 10-20% of applied dose yielded full effect; locus did not influence absorption rate, but did influence effectiveness.

(5) Solution and accumulation of DDT in epicuticular waxes of insects is deemed important. 115

(6) Insect tarsus is important in the toxicity of DDT residues to insects resting thereon. Contact of tarsus of Glossina palpalis with residues brings poisoning in 2 seconds. 2535,1453,401, 2736,1008

c) Via injection into haemolymph of Periplaneta americana DDT is distributed to alimentary tract, gonads, fat body, Malpighian tubules and thoracic muscle in large amounts and in the remaining tissues in lesser amounts; heaviest accumulation is in the fat body, alimentary canal, muscles. 559

II) Site of action in insect: [Refs.: 1226,2041,3095,2688,2687,2686,520,845,381,277,3386,3278]

a) Typical symptoms of DDT poisoning in insects are neuromuscular in origin.

b) It has been postulated, and supported by nerve potential studies, that tremors of DDT poisoned Periplaneta are due to an intense, patternless bombardment of motor neurons by impulse trains originating in sensory endings as a result of DDT action on unidentified nerve structures.

c) DDT has no significant action on the CNS.

d) Symptoms of DDT poisoning: In Periplaneta americana (sequence of appearance):
A) Hyperextension of legs, difficulty in maintaining posture; B) increasingly intense tremors of head, body, appendages; C) ataxia, hyper-reflexia to stimulus; D) inability to remain upright, turn-over; E) with insect immobilized on its back continuing leg movements viz., high frequency tremors with superimposed slow flexion and extension; F) disappearance of tremor, leaving isolated residual movements, for example, of mouth parts, antennae; G) paralysis, with heart beating for a day or more until death.
(1) The foregoing symptoms, for example tremors, leg movements were not affected by: Decapitation before or after DDT application; section of ventral nerve cord connectives caudad or cephalad of mesothoracic ganglion; mesothoracic transection; mid-sagittal section of mesothoracic ganglion; application of nicotine to the nerves.
(2) The following interventions suppress, or sharply reduce the typical symptoms of leg hyper-activity: Removal of mesothoracic ganglion; section of leg nerves laterally; application of nicotine to mesothoracic ganglion. Phenobarbital suppresses DDT tremors (Drosophila virilis) in intoxicated insects and phenobarbital pre-treatment prevents their development upon DDT exposure.

e) In the case of low dosages of DDT an intact reflex arc seems required to permit the development of the leg symptoms. Very large doses appear to exercise direct action on motor fibers. Some direct action on the myoneural junction is evidenced by the response to DDT of amputated legs (legs completely enervated, with ganglia destroyed).
(1) Direct application of DDT to the isolated nerve cord yielded no change in electrical activity.
(2) DDT at 0.01 ppm injected into Periplaneta femur yields sharp repetitive, high frequency, (300-400/second) trains of impulses over single fibers, which may be recorded from the crural nerve.
(3) In crustacean nerve axons DDT multiplied the response to single electrical stimulus, giving prolonged bursts of impulses reflected in tetanic contraction of the innervated muscle.

f) The neuromuscular action of DDT has been summarized as follows:
When DDT in contact with an insect penetrates to the sensitive parts of the nerve system, it sets up impulse trains triggered by any stimulus and the insect passes into a state of intense hyperactivity and dies, ultimately, of exhaustion.
(1) Oryzaephilus surinamensis, DDT treated, respires to about the same extent as the starving insect. Breakdowns from hyperactivity may play their part in the mechanisms of death. The poisoned insect, because of hyperactivity, cannot eat and energy reserves are rapidly depleted.
(2) Caterpillars, DDT treated, which begin to eat almost always recover. Glucose, in DDT-treated cockroaches, prolongs life.
(3) The poisoned insect "burns out." This theory explains the symptoms of initial, rapidly developed stimulation and hyperactivity, followed by a slow death in paralysis.

III) Anatomical evidences of DDT poisoning:
a) Histological signs directly attributable to DDT in insects are notable by their absence. 3345,353,2600
(1) Some effects of a cytological nature on neurons and muscle cells of a cytological nature are reported by some. 1422,519
(2) Applied to first abdominal prolegs of Heliothis armigera, DDT produced no histological effects demonstrable in nerve or other tissues. Chromatin clumping in nuclei of fat-body cells was noted. 502
(3) No demonstrable effects on the gross or fine structure of nerve cord or other tissues, were remarked. 2600

IV) DDT and temperature effects: [Refs.: 3189,2326,2011,2016,2532,2598,1305,1561,2536,965,1329,1708]
a) A negative temperature coefficient, with insects more susceptible to DDT at low than at high temperatures, has been demonstrated for several species. The effect was first demonstrated on adult Musca domestica using DDT contact sprays.
(1) Effect apparently obtains regardless of route of application:

Periplaneta americana	♀	Topical	LD_{50} 5 days	5-10	μg/insect at 15°C	3189
" "	"	"	" "	75-100	μg/insect at 35°C	
" "	"	Injection	" "	2-3	μg/insect at 15°C	
" "	"	"	" "	20-25	μg/insect at 35°C	

(2) For Tribolium castaneum adults the LC_{50} of DDT, in refined white oil, in post-treatment temperature of 80°F = 0.95% w/v and at 65°F storage was 0.36% w/v, the potency, under conditions of cold before and after treatment, being 2.61 times that observed under conditions of warm storage of insects before and after treatment. 2532
(3) For Blattella germanica topical LD_{50} at 32°C = 40.8 μg/insect; at 22°C = 12.9 μg/insect; at 14.5°C = 2.1 μg/insect. 1305
(4) Calliphora erythrocephala at 20°C markedly resists DDT poisoning by topical application; if treated with DDT, exposed for 2 hours at 36°C, and then restored to 20°C, toxic symptoms rapidly appear which disappear on removal of the insects once more to 36°C. Similar reversibility was demonstrated for Periplaneta at 15°C and 35°C temperatures. 3078
(5) In Aëdes aegypti larvae the temperature coefficient for DDT, by injection, is claimed to be positive: 1 μg/g at 15°C yielded 75% mortality and at 30°C 88% mortality; 0.5 μg/g at 15°C yielded 60% mortality and at 30°C 70% mortality. This effect was the reverse of that found in the case of larvae exposed to DDT in suspension in the larval environment. 1628

V) DDT and enzyme systems: [Refs.: 66,2724]
a) Numerous claims have been advanced of inhibitory effects of DDT on various enzyme systems:

(1) At 10^{-3}, 10^{-5} M DDT is reported to inhibit completely cytochrome oxidase from Periplaneta coxal 2305
muscle in in vitro systems, as measured by O_2 uptake in Warburg's apparatus.
(2) At 10^{-4}, 10^{-6} M, inhibition of carbonic anhydrase is claimed by some and denied by others, to account 3102
for DDT toxicity in insects. 1755
(3) In vitro or in vivo inhibition of acetylcholine esterase by DDT was not demonstrable. 2599,3096,1984

VI) DDT and respiration:
a) The oxygen uptake of DDT poisoned insects is markedly increased. 1441,353,2231,
2041

(1) DDT, at 100 μg/insect by injection in Blattella germanica brings immediate increase in O_2 uptake to 1441
3xs normal in $\frac{1}{2}$ hour during the stage of hyperactivity; with onset of paralysis O_2 consumption declines 3095
rapidly (ca. 1 hr. after treatment) and continues to decline to the time of death. In the final stages of
paralysis, respiration is probably by diffusion only.
(2) DDT, like lindane, pyrethrins, DNOC proved a stimulant of respiration (O_2 uptake) in adult Oryzaephilus 2041
surinamensis dusted with toxic concentrations of DDT. Various analogues of DDT including DDD,
methoxychlor, DFDT, dibromo-DDT, diiodo-DDT, etc., gave similar response. Only toxic concentrations
yielded the response; sub-lethal concentrations had no effect. Total O_2 uptake of treated insects and
controls showed no significant differences and it was assumed that in starvation DDT and its relatives
do not influence total respiration.
(3) Similar results have been obtained in case of Phormia regina adult and larva. Popillia japonica larva, 383
Tenebrio molitor adult. The enhanced respiration was associated always with the hyperactive phase 2055
of intoxication. Depletion of body reserves and carbohydrates content, glycogen, glucose, fat, water, 2224
has been noted. Prevention of muscle tremors in Tenebrio with narcotics suppressed the increased
O_2 uptake.

VII) DDT, metabolic fate: 2022
a) DDT is metabolized in insects. For example, Oncopeltus fasciatus (a DDT tolerant insect) rapidly 985,2975,430,
metabolizes injected, sub-lethal doses given in acetone; DDE is metabolized, as is DDA. 2708,2474
(1) Periplaneta americana metabolizes DDT to 2,2-bis-(p-chlorophenyl)-1,1-dichloroethylene (DDE) 3189
and other metabolites. Using C^{14} labelled DDT, 80% of the radioactivity in the feces is due to 2675
metabolites containing the diphenyl moiety of DDT, $<10\%$ of radioactivity is due to DDE, DDT or 2976
DDA (2,2-bis-(p-chlorophenyl) acetic acid; $<1\%$ of DDT injected or topically applied is excreted as 430
$C^{14}O_2$ in experiments conducted at 28°C on adult ♀ insects. The fecal metabolites tested vs. Musca 2708
are < toxic than DDT. Thus in addition to DDE (an)other metabolite (s) must be present containing 2022
the diphenyl-ethane structure, as well as other compounds.
(2) In Periplaneta, 72 hrs. after dosage with C^{14} labelled DDT, the radioactivity was concentrated following 2675
topical application in foregut, hindgut, fat body, Malpighian tubules. After injection of DDT into blood 559
stream it could be found in alimentary tract, gonads, fat body, Malpighian tubules, thoracic muscle, and
other tissues, with metabolism of DDT to DDE apparently taking place in all the tissues of distribution.
(3) In Epilachna varivestis DDT is broken down to DDE, but neither DDT or DDE is excreted and further 2975
degradation is indicated. Topically applied DDE, is degraded to unknown substances. This insect is
tolerant of DDT, penetration being slow and matched, very likely, by detoxification.
(4) In Argyrotaenia velutinana larva, topical DDT enters slowly via the cuticle, and is rapidly excreted by 2975
the gut after oral administration. The foregoing, plus rapid metabolism (DDE is excreted) and detoxification prevents DDT accumulation in body, The insect is DDT tolerant.
(5) In Melanoplus femur-rubrum and M. differentialis which resist topical and oral (but not injected) DDT, 2975
metabolism in gut and cuticle, with consequent detoxification, yields DDE. Further degradation of DDE
to unknown substances is indicated for M. femur-rubrum. Much of the DDT in oral dosage is excreted
unchanged in feces.
(6) In DDT-S Musca domestica, metabolism of DDT to DDE occurs, but the detoxification is not swift 2974
enough to forestall the accumulation and lethal action of DDT at its site of action.
(7) Trogoderma larva, naturally tolerant of DDT, is reported not effectively to alter DDT metabolically. 3332
(8) The nature of the metabolite(s) which in treated insects is (are) supposed to represent that part of the 3189
applied dose not recoverable as DDT or DDE remains unknown. In Periplaneta this (these) unknown(s), 2976
stable to KOH and H_2SO_4 behaved somewhat like p,p'-dichlorobenzohydrol. DDA (2,2-bis-(p-chloro- 3292
phenyl) acetic acid), the principal water soluble metabolite in rabbits, is seemingly not the unknown 3334
factor. Musca domestica, treated topically with DDA, yielded 95-100% of the total dose as a salt 3332
within 30 hours. 430,2708
b) Metabolism of DDT in DDT-R insects: (Also see Addendum) 2233
(1) Degradation studies of C^{14} labelled DDT in 7 DDT-R Musca domestica biotypes showed DDE, 2474
(2,2-bis-(p-chlorophenyl)-1,1-dichloroethylene) to be the sole significant product of DDT metabolism.
Both DDT and DDE were present in ether soluble fecal fraction. Ratio of DDE: DDT increases with
time after dosage. Very small amounts of radioactive product(s) appeared in the water soluble fecal
fraction.
(2) An enzyme from tissues of DDT-R Musca domestica catalyzes the dechlorination of DDT to non-toxic 2971
DDE. The enzyme appears to require glutathione as activator and is irreversibly inhibited at pH 3.5
or less with maximum activity at ca pH 7.4; temperatures much >37°C (e.g. 43°C) reduce the enzyme
activity to vanishing point; at 27°C activity is ca. 50% that at 37°C; rate and time characteristics of
continued enzyme action were better maintained under nitrogen than under air; the enzyme is highly
specific, attacking only those analogues of DDT which are sterically similar to it; the enzyme appears
in all DDT-R biotypes examined but not in DDT-S biotypes.

c) Action of certain "synergists" on DDT effects and metabolism:

(1) Piperonyl cyclonene (q.v.) applied simultaneously with DDT to DDT-R Musca biotypes was reported to potentiate the action of DDT and reduce the ability of the DDT-R insect to detoxify DDT. 2478 1591

(2) In *Periplaneta americana*, piperonyl cyclonene is said to inhibit absorption of DDT and metabolite excretion. 2675

(3) Certain non-insecticidal DDT analogues are > effective than piperonyl cyclonene in potentiating DDT action in DDT-R *Musca* biotypes. Some of these "synergists" inhibit the DDT-dehydrochlorinase of DDT-R flies *in vitro*. 2091 2299

(4) Di-(p-chlorophenyl) methylcarbinol (DMC), q.v., potentiates DDT vs. DDT-R *Musca*. It is suggested that the synergist competes with DDT for the DDT detoxifying agent (s) in the fly. DMC inhibits DDT-dehydrochlorinase *in vitro*. 2473 2299

(5) The non-insecticidal DDT analogues which potentiate DDT action on DDT-R *Musca* biotypes have no potentiating action whatsoever on DDT-S biotypes. 2091 2299

(6) Effects of piperonyl cyclonene on mortality and degradation of DDT to DDE as measured 24 hrs. after topical application to several DDT-R biotypes of *Musca domestica*: 1591

Biotype	Toxicant Applied (per Fly)	% Kill	Internal DDT in living flies µg/fly	Internal DDE in living flies µg/fly	Toxicant Applied	% Kill	Internal DDT in dead flies µg/fly	Internal DDE in dead flies µg/fly
Berkeley	0.1 µg DDT	95	0.02	0.03	0.1 µg DDT + 5 µg PC*	80	0.02	0.01
Laton	0.5 " "	51	0.01	0.24	0.5 " " + 10 µg "	100	0.11	0.01
Super-Laton	2.5 " "	49	0.12	1.12	2.5 " " + 10 " "	100	0.5	0.19
Bellflower	5.0 " "	42	0.29	1.58	5.0 " " + 25 " "	88	0.72	0.25

*=Piperonyl cyclonene. Piperonyl cyclonene apparently inhibits conversion of DDT to DDE.

(7) Distribution of DDT, DDE after topical application of 50 µg DDT + 25 µg piperonyl cyclonene/insect to *Musca*, Bellflower biotype: 1591

Site of Application	DDT (µg) in Head	DDT (µg) in Thorax	DDT (µg) in Abdomen	DDE (µg) in Head	DDE (µg) in Thorax	DDE (µg) in Abdomen
Head	0.1	0.066	0.020	0.001	0.033	0.035
Thorax	.004	.119	.061	.008	.029	.048
Abdomen	0	.049	.138	.002	.024	.061

DDT tends to remain in the segment of application but with some internal distribution elsewhere; DDE is always found in the abdomen regardless of DDT application site.

(8) DDT and other compounds: Action with synergists vs. *Tribolium castaneum*: 1509

Exposure To	Insecticide	Adjuvant (Synergist)* PB	PC	SC	NPI	OBD
Film (residual)	DDT	—	0	0	—	(+)
" "	Pyrethrins	+	+	+	+	0
" "	Lindane	(+)	0	(+)	0	0
Contact Spray	DDT	0	0	+	—	(+)
" "	Pyrethrins	+	+	+	+	0
" "	Lindane	+	+	+	(+)	0

*PB=piperonyl butoxide, PC=piperonyl cyclonene, SC=n-octyl sulfoxide of isosafrole, NPI=condensation product of isosafrole + n-propyl maleate, OBD=n-octyl bicycloheptene dicarboximide; +=marked synergism, (+)=slight synergism, 0=no effect, — = marked antagonism.

VIII) DDT and resistance thereto: (also see the general treatment titled Resistance)
[Refs.: 2233,148,153,2223,373,3057,423,1597,2376,1762,2434,2723,2274,374,372,1805,2021,2096,2097,2558,2972,230, 282,438,763,765,972,1091,1803,2052,1975,1361].

a) Biotypes resistant to DDT have appeared among wild or field "populations" of several insect species and resistance has been elicited experimentally from originally DDT-susceptible biotypes by successive generations of exposure and selection.

(1) Among the insect genera and species in which resistant biotypes have been observed among field or wild "populations," subjected to the selection pressure of DDT exposure over periods of time, are: *Musca*, *Aëdes*, *Culex*, *Anopheles*, *Pediculus*, *Psychoda* (family), *Cimex*, *Carpocapsa*, *Pieris*, *Leptinotarsa* (?), *Pulex*, *Plutella*, *Blatta*, *Triatoma*, *Boöphilus*, *Erythroneura variabilis*, *Trichoplusia*, *Lygus*, *Sceleroracus vaccinii*, *Rhopobota naevana*, *Drosophila*.

(2) Resistance of various *Musca*, and mosquito, biotypes is perhaps the most intensively studied.
[Refs.: 2723,2274,372,2434,1805,2021,2097,2558,2972,230,282,438,763,765,972,1091,2052,1803,1193]

b) Tabulations to illustrate the trend of DDT resistance (tolerance) development in field and laboratory; *Musca domestica*:

Year	Field				Laboratory LD_{50} 24 hrs, Topical (μg/fly) At 80°F
	Danish Farm*		Farm I	Farm II	
	No. Sprayings with DDT	Estimated Control (%)	LD_{50} 24 hr, Topical (μg/fly) At 80°F		
1945	?	ca 100	0.2	0.18	0.33 (original strain) ↓
1946	several	decreasing	0.3	0.4	18 generations exposure of original strain and descendants to maximum DDT levels ↓
1947	several	decreasing	0.8	0.7	
1948	?	ca 0**	8.1	9.0	>100μg/fly (DDT-R biotype)

*Flies breeding abundantly in calf boxes of treated cow sheds.
**Ca 100% control yielded by BHC.

c) Development of resistance in mosquito "populations:"

(1) Increased tolerance of mosquitoes to DDT has been recorded for various species in many parts of the world, among the species: *Culex pipiens*, *Culex quinquefasciatus*, *Culex tarsalis*, *Aëdes nigromaculis*, *Aëdes dorsalis*, *Aëdes taeniorhynchus*, *Aëdes sollicitans*, etc.

(2) The tolerance is manifested by both larvae and adults and many times the rate of application of DDT once controlling no longer yields control.

d) Resistance in insects of public health importance other than flies and mosquitoes:

(1) Strains of lice (*Pediculus humanus corporis*) in Korea were observed to tolerate maximal concentrations of DDT in dusting powders. These biotypes retained their sensitivity to lindane, pyrethrins, toxaphene. 915

e) Experimental confirmations, observations, interpretations:

(1) In *Musca domestica*, intensive inbreeding and selection of "populations" in which adults and larvae have been constantly exposed to DDT, lead to the appearance of biotypes tolerant in greater or lesser degree to DDT when compared to the "population" of origin. This comprises selection by exposure, over several generations, of adults and larvae to DDT and the repeated inbreeding of the survivors. Continued exposure eliminates susceptibles with consequent inbreeding of relatively tolerant survivors. By constant selection, and inbreeding, in presence of DDT, intensification and fixation of the factors responsible for tolerance occurs, until maximum tolerance is attained. Genetically speaking, in terms of tolerance to DDT, homozygosity for resistance is achieved in step-wise fashion. Exposure of adults and larvae, intensifies the selection process. 373

(a) Experimental establishment of tolerance, during the early generations of exposure, proceeds slowly. Once resistance has appeared the tolerance is rapidly enhanced to its maximum under the continued pressure of selection. Finally, resistance is raised to such levels that the selected biotype(s) may be maintained in a heavily DDT-treated environment.

(b) DDT tolerance, once established, persists. A field biotype resistant to DDT showed no tolerance loss 2 years after the exposure to DDT was discontinued. Laboratory resistant biotypes in absence of outbreeding have, with no further DDT exposure, held their tolerance at a constant level for >30-50 generations. Reversions from tolerance to susceptibility have, however, been noted.

(c) Resistant biotypes, whether field collected or produced by selection in the laboratory, have often proved markedly tolerant of DDT analogues and other chlorinated hydrocarbon insecticides to which they had never been exposed ("cross-tolerance").

(d) Genetically, the phenomenon of resistance to DDT appears to be one of multiple factor inheritance, and the loci involved are not sex-linked but borne by both sexes. Crosses yield a "blending inheritance" of resistance characters which may persist, in absence of further DDT exposure, without change through as many as 15 generations.

(e) DDT tolerance in some resistant *Musca* biotypes accompanies the ability to metabolize (detoxify) DDT more or less rapidly and completely to non-toxic or markedly less toxic substances.

(f) Other physiological differences, for example, development rate, size and behavior, may distinguish the resistant biotype from the ordinary "wild-type" strain(s).

(2) In *Drosophila melanogaster* successive spraying with DDT suspension of adults of a wild colony and 3057
their surviving progeny, through several generations yielded, as in *Musca*, resistance to DDT. The 2223
rate of development of resistance depended: a) On the relative proportion of resistant to susceptible 2389
individuals in the original "population;" b) intensity of selection as measured by DDT concentration, mortality rate, or both. Two premises are available to account for the facts: I) Natural selection working on available genetic variability in heterogeneous (heterozygous) "populations" leads to increasing gene frequency of resistance-conferring factors; II) Direct response (*ad hoc* response) of adaptation by the insect to the insecticide in which case the homogeneity or heterogeneity of a "population" should not matter.

(a) Experiment proves that:

I) The ability to become DDT-resistant is related to the genetic variability of the original stock.

II) Failure of certain "populations" derived from intensely inbred stocks, hybrid or laboratory in origin, to develop enhanced tolerance to DDT, indicates that the proper genes must be present in the original "population" subjected to DDT selection pressure, for resistance to appear.

III) Resistance development is directly related to selection pressure.

IV) Resistance usually increases most rapidly during the first few months of selection.
V) Each stock subjected to selection tends to have, finally, a level of resistance different from other stocks.
VI) Resistant stocks differ from each other and from controls.
VII) Resistance level does not necessarily remain static; 3 resistant "populations" were noticed to undergo a decline in resistance despite continued exposure to DDT. Such populations may have failed to attain homozygosity for the factors conferring resistance or may have undergone mutation to susceptibility at one or more of the loci involved.

f) Biochemical factors in DDT tolerance:

(1) Ability of certain DDT-R biotypes to convert DDT to DDE, *Musca domestica*: 1591

Biotype	Topical DDT Applied (μg/fly)	Condition After 24 hrs	DDT Recovered (μg/fly)	DDE Recovered (μg/fly)
Berkeley	0.05 (LD_{50})	Dead	0.026	0.024
		Living	0.015	0.033
"	2.0	Dead	0.371	0.034
Laton	0.5 (LD_{50})	Dead	0.127	0.107
		Living	0.005	0.241
Super-Laton	2.5 (LD_{50})	Dead	0.294	0.643
		Living	0.120	1.121
Bellflower	5.0 (LD_{50}=7.4 μg)	Dead	0.520	0.967
		Living	0.292	1.576

Total DDE formed varies directly with LD_{50}.

(2) Rate of absorption of DDT by DDT-R and DDT-S biotypes: 1591

Time (hrs)	DDT Topical (2 μg/fly) % Absorbed By		
	Berkeley*	Super-Laton	Bellflower
2	32	42	45
12	57	72	74
24	63	85	85

*All dead at 12 hrs.

DDT-R biotypes appear to absorb DDT more readily than DDT-S biotypes. Temperature influences: In Bellflower 24 hr absorption at 13.5°=18.4%; 26°=67.4%; 32.5°=71.2%; % mortality is in opposite order.

(3) Amount DDT and DDE in Bellflower (DDT-R biotype) at various times after 5.0 μg/fly topical. 1591

Time After Exposure (hrs)	(μg/fly)			
	External DDT	Internal DDT	Internal DDE	Unaccounted For
24	2.154	0.288	1.718	0.839
48	1.6	0.189	1.756	1.455
72	0.969	0.103	1.311	2.707
96	0.732	0.143	1.871	2.254

(4) DDT and DDE, from larvae, pupae and adults of Bellflower (DDT-R strain), reared in a larval medium containing 0.5% DDT, a dosage which permits but 50% pupation and pupal emergence: 1591

Stage	Age (days)	DDT Recovered (μg/fly)	DDE Recovered (μg/fly)
Larva	3	2.81	21.89
Larva	6	0.64	14.34
Pupa (early)	7	0.41	10.45
Pupa (late)	11	0.35	10.03
Adult (just emerged)	12	0.33	9.94
Adult (3 days old)	15	0.21	9.53
Adult (6 ")	18	0.09	6.65

(5) DDT and DDE in tissues of 3 day old adult flies reared as above, Bellflower biotype: 1591

Tissue	DDT μg/fly	DDE μg/fly	Ratio
Cuticle	0.2	11.1	55
Gut	0.07	1.6	23
Fat Body	0.14	2.8	20
Muscle (thorax)	0.06	0.9	15
Nerve Cord	0.04	0.6	15
Blood	0.03	0.1	3

Cuticle, fat body (+ ovary) are the apparent chief depot sites of DDT. Integument appears to be the site of conversion of DDT to DDE.

(6) Summary of biochemical differences between DDT-R and DDT-S *Musca domestica*:

(a) Initial absorption rates of topically applied DDT reported not to differ significantly in DDT-R and 2972
DDT-S biotypes. 3337

(b) Detoxification: 2974,3043,

I) In DDT-R biotypes: 24 hrs after topical application ca. 35% of applied DDT remained 2015,1597,
unabsorbed on surface, 5% unchanged DDT was within the insect widely distributed but with 3337,3338,
concentration in fat body. Of the rest of the applied dose (60%) ca 30% was recoverable as 420,2094,
DDE concentrated in cuticular hypodermis in which the chief site of detoxification, by con- 2096,2097,
version of DDT to DDE by the enzyme DDT-dehydrochlorinase, is believed to be. This 3332,2971,
enzyme also dechlorinates DDD and methoxychlor and may account for the cross-tolerance 2973,1078,
of DDT-R biotypes for these toxicants. The remaining DDT proved recoverable by thorough 2474.
extraction of tissues. DDE appears to be the sole metabolite of DDT.

II) In DDT-S biotypes topically applied DDT rapidly enters the body to appear in largest con- 1933,2013,
centration in Malpighian tubules and gut as DDT unchanged. Very slight conversion to 2477,3332,
DDE has been demonstrated in absence, however, of any demonstrable DDT-dehydro- 2971,2974,
chlorinase. 3043.

III) The ability to detoxify DDT by conversion to DDE is accepted by some as the major factor 2476
presently demonstrable to account for DDT tolerance in DDT-R biotypes. Storage of DDT in 2475
body parts where it is relatively harmless is also considered to play a part in tolerance, since 152
unchanged DDT could still be recovered from DDT-R biotypes in amounts sufficient to kill 2971
susceptible flies, in spite of the high efficiency of the detoxifying mechanism. Some believe
that other factors are, at least in part, at play.

(c) Respiration, O_2 uptake:

I) DDT-S biotypes of *Musca* respond to DDT by a pronounced increase in O_2 consumption during 1078
the phase of hyperactivity. DDT-R biotypes are reported to show a much lower degree of
stimulation of O_2 uptake than DDT-S biotypes at equivalent dosages.

(d) Synergism:

I) The role of certain synergists in blocking the detoxifcation mechanisms competitively with DDT has been discussed above.

(e) For additional tabular evidence of resistance to insecticides among insects and general considerations see the section titled, Resistance.

7) Field experiences in the control of insects with DDT:

a) Reports of field experiences with DDT are too numerous to permit review here. Those interested will find excellent treatment of this aspect in such periodicals as the "Journal of Economic Entomology," "Agricultural Chemicals," "Soap and Sanitary Chemicals," "Annals of Applied Biology," etc., from the year 1940 onward.

Addendum; recently published data:

1) Metabolism of C^{14} labelled (radioactive) p,p'-DDT by *Leucophaea maderae* (adult ♀) and *Pyrausta nubilalis* 2022
(5th Instar larva):

a) *Leucophaea maderae*:

(1) Topical DDT was rather slowly absorbed, ca 90% applied dose in 20 days.

(2) 50% of total DDT applied was excreted over period of 36 days.

(3) Paper chromatographic separation of radioactive compounds in the feces revealed: Presence of DDT, DDE, and 3 unidentified metabolites, with DDT predominant during first 24 hours after treatment, after which a metabolite with an R_f value of 0.88 was the major radioactive compound excreted (see proposed pathway schema below).

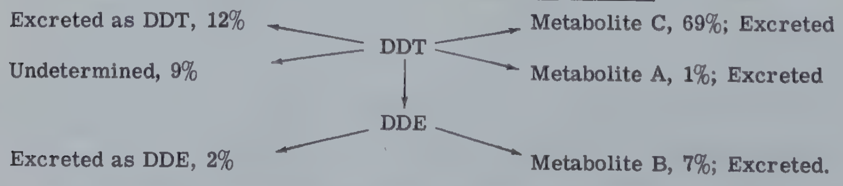
b) *Pyrausta nubilalis*:

(1) Reveals some tolerance of DDT with the conversion of significant amounts of absorbed DDT to DDE.

(2) By colorimetric and radiometric analysis no metabolite other than DDE proved demonstrable.

(3) 15% of the total applied dose was absorbed in 120 hours.

c) Proposed metabolic schema for DDT in *Leucophaea maderae* ♀ (adult)


Excreted as DDT, 12%
Metabolite C, 69%; Excreted
DDT
Undetermined, 9%
Metabolite A, 1%; Excreted
DDE
Excreted as DDE, 2%
Metabolite B, 7%; Excreted.

2) Temperature and Life Cycle Stage, Effect on Toxicity and Metabolism of DDT in *Musca domestica*; Menn, J.J., et al., The Journal of Economic Entomology 50(1): 67, 1957:

a) 25 ppm DDT in larval diet of a DDT-S biotype (Stauffer strain) yielded >1 µg DDT and DDE/adult fly with 30% of the insects dead soon after emergence from pupa.

b) 25 ppm DDT in larval diet of a DDT-R biotype (Bellflower strain) yielded ≪DDT and >DDE in the emerged imago and no mortality.

(1) DDT at 2000 ppm in larval food yielded 100% kills of DDT-S larvae.

(2) DDT at 2000 ppm in larval food (DDT-R biotype) yielded larvae containing less than 1 μg DDT/insect with decrease to unappreciable amounts in the imagos; in larvae DDE was present at 9 μg/larva, decreasing to 3.5 μg/imago. Mortality was 30% of the emergent imagos.

c) LD$_{50}$, DDT in oil, DDT-S biotype: At 15°C 0.052 μg/fly; at 25°C 0.112 μg/fly; at 35°C 0.252 μg/fly.
LD$_{50}$, DDT in oil, DDT-R biotype: at 15°C 1.6 μg/fly; at 25°C 3.84 μg/fly; at 35°C 7.8 μg/fly.
(1) Temperature coefficients are uniformly negative and vary from 2.0 to 2.4.

d) Absorption by adult Musca of DDT in oil increased with temperature (but the influence of temperature was less than that on absorption from dry deposits).

(1) Initial absorption differences at 35°C and 25°C fade out within 24 hrs., and by 48 hrs. total absorption is the same at 15°C, 25°C, 35°C.

(2) Rate of DDT metabolism is of particular importance in the first few hours; % of absorbed DDT metabolized at 35°C:

At Hr(s)	DDT-R	DDT-S
1	48%	3.6%
2	67%	15 %
4	74%	23 %

(3) After a few hours the temperature coefficient (35°C/15°C) of DDT metabolism increased steadily while the coefficient of absorption decreased. Thus it is concluded that if a fly lives for a few hours at the higher temperature the chances of its survival are enhanced. Increased temperature favors survival whenever exposure conditions are such that after a short interval the rate of detoxification or excretion exceeds the rate of intake unless single exposure dosages are so great that death of the insect occurs within a few hours. Massive doses always have a positive temperature coefficient.

3) Toxicity of DDT in acetone and in oil solutions for adult Musca domestica; Barker, R.J., and Abd-el-Rahman Rawhy, The Journal of Economic Entomology 50(1): 105, 1957:

a) Mortality of 2 day old adult Musca (imago) NAIDM biotype treated with DDT in redistilled acetone and Shell Risella Oil 117 applied by the measured drop method to the pronotum with holding temperature at 25.5°C, R.H. 30%:

LD$_{50}$, 24 hrs. (μg/fly)	
DDT in acetone	DDT in oil
0.134 (0.127-0.142) slope 6.19 ± 0.56	0.566 (0.475-0.675) slope 9.26 ± 0.45

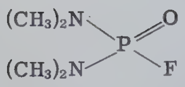
b) Imagos of a DDT-R biotype treated with 0.8 μg DDT in 1.23 μ liters of acetone yielded a mortality of 1.7% (904 subjects); following 0.8 μg DDT in 1.23 μ liters oil, 21.2% of 695 subjects succumbed in the biotype ordinarily DDT immune. Oil alone yielded a 0.5% mortality (195 subjects).

(1) A highly DDT-R biotype treated with 0.8 μg DDT in 1.23 μ liters solvent, 24 hrs exposure yielded the following: 74.1 ± 14.6% absorbed in case of DDT in acetone and 40.7 ± 11.9% in case of DDT in oil. Estimated absorption of the LD$_{50}$ 24 hrs. in acetone (see above)=98% and of the LD$_{50}$ 24 hrs. in oil (see above) = 65%.

c) DDT, topically applied in acetone is 4.2 times as toxic to Musca imagos when compared with DDT in petroleum oil; dosage-response curves are not parallel. On resistant biotypes 0.8 μg DDT in oil proved more toxic in oil than in acetone. More DDT was absorbed from acetone than from oil solution with the difference apparently insufficient to explain the differences in mortality.

18

BIS-(DIMETHYLAMINO)-FLUOROPHOSPHINE OXIDE
(Bis-(dimethylamino)-fluorophosphate; BFPO; Dimefox; Hanane.)



Molecular weight 154

GENERAL [Refs.: 2118,2128,353,2231,665,554,2769,2252,2253,1415,2942,2773]

An aminofluorophosphate insecticide of the general group of organophosphorus insecticides (see the general treatment of). Closely related to Mipafox (Isopestox®), q.v. Possesses high systemic insecticidal powers in control of beetles, caterpillars, aphids, etc., but treated crops have been deemed too toxic for human consumption. Solutions, at 0.02-0.05% in water applied to the roots of plants render the juices and tissues insecticidal—a property referred to by Schrader as a "chemo-therapeutic" effect and by Martin as a "systemic" effect.

PHYSICAL, CHEMICAL

A colorless, mobile liquid of faint odor; vapor is intensely poisonous; $d_{4°}^{20°}$ 1.12; b.p. 67°C^{4}mmHg, 96°C^{18} mmHg; 2651
v.p. 0.18 mmHg at 15°C, 0.36 mmHg at 25°C, 0.4 mmHg at 30°C; volatile, with a vapor concentration at 25°C of 2231
2200 mg/m^3, a 15°C of 1130 mg/m^3; evaporation constant 0.2$^{15°}$ C; miscible in water and most organic solvents; half-life at pH 4=8.6 days, at pH 6= 2 years, at pH 8= >10 years; in vitro a weak anticholine esterase agent.

TOXICOLOGICAL

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	7.5		2410
Rat	ip	LD_{50}	5.0		861
Mouse	sc	LD_{50}	1.0	bis-diethylamino-* 160 mg/k bis-dibutylamino-* 16 mg/k bis-dicyclohexylamino-* 9 mg/k	2231
Mouse	ip	LD_{50}	5.0		861
Mouse	ip	LD_{50}	1.4		2410
Guinea Pig	ip	LD_{50}	2.5		2410
Dog	iv	LD_{50}	5-10		2410

*fluorophosphine oxide

a) Weak in vitro capacity for choline esterase inhibition; the conversion to highly toxic substance (s) occurs metabolically in the susceptible animal body. 1415

b) Residues (toxic): 0.1 ppm deemed a "nil" residue in cocoa by U.S. Food and Drug Administration; analytical methods detect residues of 0.02 ppm. 2651

   (1) As concerns toxic residues, it is the original substance BFPO which is significant and not the metabolites or breakdown products thereof. 1415

2) Phytotoxicity:

a) Its use as a systemic insecticide would imply a relatively low phytotoxic potential. Phytotoxicity for grape foliage is reported. 2651 1375

   (1) May be sprayed upon plant foliage (wasteful because of the high vapor pressure.)
   (2) May be applied to the trunks of trees to be treated.
   (3) May be applied to the roots by watering or the implantation in soil of soluble capsules containing the insecticide.
   (4) Not phytotoxic for cocoa or coffee plants; no phytotoxicity observed for other plants. 1374,1375

3) Toxicity for insects:

a) Results reported on the use of Hanane vs. plant pests: 1700

Plant	Pest	Type of Experience	Concentration Used	Type Of Application	Result	Place Of Experience
Plum	Anuraphis padi	Field	0.017%	Foliage Spray	good control	United Kingdom
Strawberry	Capitophorus fragaefolii	Field	0.06%	Foliage Spray	90% Kill	United Kingdom
"	Amphorophora rubi	Field	0.045%	Foliage Spray	91% Kill	United Kingdom
"	Macrosiphum gei	Field	0.045%	Foliage Spray	91% Kill	United Kingdom

Plant	Pest	Type Of Experience	Concentration Used	Type Of Application	Result	Place Of Experience
Strawberry	Macrosiphum rosae	Field	0.045%	Foliage Spray	91% Kill	United Kingdom
Currant	Eriophyes ribi	Field	0.06%	Foliage Spray	poor control	United Kingdom
Brussels sprout	Brevicoryne brassicae	Field	0.15%	Foliage Spray	99% Kill	United Kingdom
Beans	Aphis fabae	Laboratory	0.05%	Foliage Spray	100% Kill	United Kingdom
Cocoa	Pseudococcus njalensis	Field	50%	Soil	99.9% Kill	West Africa
Coffee	Pseudococcus kenyae	Field	0.36%	Soil	100% Kill	East Africa
Cotton	Hercothrips fumipennis	Field	10lbs/acre	Irrigation H_2O	97% Kill	Sudan
Mangold	Myzus persicae	Field	0.05%	Foliage Spray	100% Kill	United Kingdom
Sugar beet	Myzus persicae	Field	0.2%	Foliage Spray	98% Kill	United Kingdom
Tulip	Macrosiphum euphorbiae	Field	0.02%	Foliage Spray	98% Kill	United Kingdom
"	Aulocorthum circumflexum	Field	0.02%	Foliage Spray	98% Kill	United Kingdom
"	Aulocorthum solani	Field	0.02%	Foliage Spray	98% Kill	United Kingdom
"	Masonaphis rhododendri	Field	0.02%	Foliage Spray	98% Kill	United Kingdom
"	Myzus ascalonicus	Field	0.02%	Foliage Spray	98% Kill	United Kingdom
"	Myzus persicae	Field	0.02%	Foliage Spray	98% Kill	United Kingdom
"	Rhopalosiphoninum latysiphon	Field	0.02%	Foliage Spray	98% Kill	United Kingdom
Dahlia	Aphis fabae	Field	0.04%	Soil	80% Kill	United Kingdom
"	Myzus persicae	Field	0.1%	Foliage Spray	100% Kill	United Kingdom

b) Comparison of effect as a contact and a systemic insecticide. Applied as soil treatment: 2651

Concentration	Dosage Per Plant	Insect	% Mortality After: 24 hrs	10 days	20 days	30 days	40 days
0.4%	2cc	Brevicoryne brassicae	65	89	27	0	7
0.4%	5cc	" "	78	86	54	15	4
0.4%	10cc	" "	92	100	73	15	3
0.4%	10cc	Aphidius brassicae	8	4	0	0	0
0.4%	10cc	Coccinella septempunctata	7	0	0	1	0
0.4%	10cc	Syrphid larvae	0	1	0	0	0

c) Effect on natural predators of Brevicoryne brassicae: 2651

(1) On plants sprayed with a 0.4% solution at 2cc/plant.

(2) Compare with the foregoing table.

Predator	% Mortality After: 24 hrs	10 days	20 days	30 days	40 days
Brevicoryne brassicae (prey)	100	88	62	21	9
Coccinella septempunctata	100	12	2	0	0
Aphidius brassicae	100	4	0	0	0
Syrphids (larvae)	100	6	0	0	0

d) Used to control pests of cocoa and coffee trees: 1374, 1375

(1) Applied to trunk, the result is a rapid uptake into the tree with a highly insecticidal effect on Pseudococcus kenyae (on coffee), and Pseudococcus njalensis (on cocoa). (Both are mealybugs of high economic importance)

(2) To control the mealybug vectors of swollen shoot virus in cocoa, Pseudococcus njalensis, P. citri and Ferrisia virgata which are protected from sprays and topically applied insecticides by "tents" constructed by nurse ants of the genus Cremogaster:

(a) Hanane gives the best systemic results, being effective in dilution, or applied to the soil directly as the concentrate.

(b) Application is made in amounts proportional to tree girth:
1.6 g/inch of girth for 5 in. trees (girth)
2 g/inch of girth " 10 in. "
2.7 g/inch of girth " 15 in. "
3.6 g/inch of girth " 20 in. "

(c) On 500 trees (3.5-18.5 in. girth) 99.9% mortality of mealy bugs was reported.

(d) Trees given 1.2 g/in. girth remained toxic for ca 5 weeks; given 1.6 g/in. girth, toxicity persisted ca. 7 weeks. Trees, treated according to the girth/weight correlation, maintained their toxicity to mealy bugs for at least 7 weeks.

(e) Pollination of flowers of the cocoa tree was not affected; this is an indispensible property in any treatment of cocoa with insecticides.

(f) Because of its toxicity to man, application of Hanane in soluble capsules implanted in moist soil at the tree base proves highly effective. 99.7% reduction in mealy bug has been achieved by this method.

(g) Toxic Residues: In cocoa pods, harvested 5 weeks after treatment, and fermented and dried, in preparation for processing, no residues were found. This does not obtain in all crops.

e) Controls grape Phylloxera at the rates used on cocoa according to some workers, but phytotoxicity to 1374
foliage has been reported. Others pronounce the treatment worthless not only on grapes vs. Phylloxera 1375
but on pests of cocoa. 755

f) Recent studies of P^{32} labelled BFPO have been made which reveal the following facts: 695,703,701
   - (1) The compound is absorbed by the roots (Phaseolus, Vicia) from hydroponic culture solutions.
   - (2) Absorption is less rapid from soil than from sand media.
   - (3) Appreciable amounts are given off by the leaves of treated plants as vapor; the transpired material is radioactive (P^{32} containing), and insecticidal by fumigant effect. The tissues of treated plants are insecticidal "systemically" aside from the fumigant effect.
   - (4) BFPO is less liposoluble than OMPA (Schradan), and does not penetrate as readily as OMPA the leaves of bean plants when applied thereto. Because of volatility, it is lost from plants by vaporization, but small amounts are translocated to various parts of the treated plant following direct application to the leaves (bean, cabbage, hops).
   - (5) Plants, treated "systemically," via the roots, for example, with BFPO, give off a toxic vapor which is capable of killing insects by straight fumigatory effect.
   - (6) A corollary of the preceding is that BFPO is less persistent (by reason of volatility of the parent substance and/or the metabolite in the plant) than OMPA.

4) Pharmacological; pharmacodynamic, physiological, etc.:

1) Not too much of a precise nature is known specifically for this compound in its mode of toxic action or 1415
biochemical activity.

a) By analogy: Hydrolysis of fluoroethoxymethane for example would yield fluoroethyl alcohol. 2157

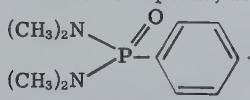
(1) Animals exposed to concentrations of 0.1 g/m³ of fluoroethyl alcohol for 10 minutes seemed un- 2157
affected, but perished within the hour in violent convulsions. 2158

(2) Fluorophosphine oxide is probably stable. However, related alkyl fluorophosphonates are extremely 2157
toxic.

(a) Exposures of human beings to 1 ppm for 5 minutes yielded severe miosis and loss of visual accommodation ability for several days. Amounts too low for chemical detsction bring blurring of vision.

(3) As in the case of OMPA, q.v., BFPO can be activated to yield an agent far more inhibitory than it- 496
self for human serum choline esterase (CHE) ID_{50} comparison: 4×10^{-8} M for activated agent; 1416
3×10^{-3} M for original BFPO. The activation comprises an oxidation, at one of the phosphoramide N atoms, which yields a phosphoramide oxide (monophosphoramide oxide), more active than the original compound vs. ChE, and with an estimated half-life, in water at room temperature, of 28 hours. The oxidative activation can be effected biochemically by mouse liver slices in vitro in presence of O_2 and at physiological temperatures. As in the case of OMPA, the reaction is believed to be enzymatic. Chemical oxidation by permanganate ($KMnO_4$) achieves the same result as the biochemical system.

(4) A related compound, bis-(dimethylamino)-p-nitrophenyl phosphate, 2244



—NO_2, while highly toxic for mammals (LD_{50} oral, mouse, 7 mg/k), proved non-toxic for Musca domestica, Apis mellifera, Periplaneta americana, and inhibited choline esterase(s) (ChE) very feebly.

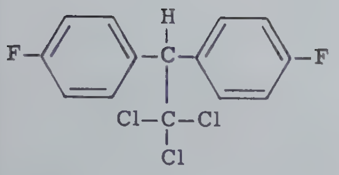
Addendum

1) Comparative toxicity of bis-(dimethylamino) fluorophosphine oxide (Dimefox ®) and other compounds to 1718
Apis mellifera by various routes of application and exposure:

Compound	Oral Dose (µg/bee To Yield Mortality Indicated In 24 Hrs.			Contact Spray Dose (µg/cm²) To Yield Mortality Indicated			Effects Of 1 Hour Contact With Residual Dry Films				Effects Of Vapors From Residual Dry Films; Exposure: 1 Hour	
	20%	50%	90%	20%	50%	90%	% Kill 24 hrs.	µg/cm²	Average Field Dose µg/cm²	Ounces/ Acre	% Kill 24 hrs.	µg/cm²
Parathion	0.018	0.04	0.144	0.144	0.257	0.354	90	0.54	1.4	2	100	5.0
							10	.18			0	2.8
TEPP	.052	.065	.093	.358	.445	.621	8	.22	5.6	8	0	5.5
Lindane	.026	.079	.346	.772	.851	.986	100	.28	2.8	4	100	.44
							0	.074			0	.28
Dieldrin	.223	.269	.354	.386	.572	1.052	90	.09	1.4	2	100	.28
							10	.04			0	.074
Aldrin	.181	.239	.365	.327	.562	1.274	75	.09	1.4	2	100	.74
							0	.04			0	.074
Chlordane	.831	1.122	1.730	3.802	5.000	7.580	100	3.4	11.2	16	100	3.7
							12	.9			0	.37
Systox®	1.256	1.478	1.884	4.321	5.123	6.619	50	10.0	—	—	0	18.5
							22	6.8				
Dimefox®	1.25	1.905	3.506	16.52	23.17	38.64	0	50.0	—	—	0	74.0
Toxaphene®	25.12	39.81	80.17	36.73	44.67	59.98	9	110.0	16.8	24	0	70.0
							0	40.0				

19

2,2-BIS-(p-FLUOROPHENYL)-1,1,1-TRICHLOROETHANE
(DFDT; 1,1,1-Trichloro-2,2-bis-(p-fluorophenyl) ethane; Difluorodiphenyltrichloroethane; Fluoro-DDT; Fluoro-gesarol; "Gix.")



Molecular weight 321.6.

GENERAL (Also consult the section on DDT) [Refs.: 2229,2466,367,415,767,1818,2040,2094,2551,3203]

A fluorine analogue of DDT in which fluorine replaces chlorine on the rings at the p,p' positions. The insecticidal action of DFDT is somewhat more rapid than that of DDT, but the residual activity is decidedly shorter. Less toxic for mammals than DDT; stated to be $\frac{1}{4}$th as toxic as DDT for rats and mice. Compared qualitatively with related substances in residual effectiveness vs. mosquitoes and houseflies: DDT > methoxychlor > methyl-DDT > DDD > DFDT. Toxicity for insects ranges from $\frac{1}{10}$th to 10 times that of DDT, depending on species and method.

PHYSICAL, CHEMICAL [Refs.: 2231,129,353,2229]

Pure: A solid in colorless, needle-like crystals; technical: A viscous, colorless liquid; the technical product contains up to 10% o,p'-isomer b.p. 135-136°C at 9 mmHg; m.p. 45.5°C; b.p. 177-178°C at 9 mmHg; v.p. 2.2×10^{-6} at 20°C; odor resembles that of ripe apples; may be considered insoluble in water; moderately to readily soluble in most organic solvents, for example, in g/100cc solvent at 27°C: Carbon tetrachloride: 650; cyclohexanone: 850; dibutyl phthalate: 260; o-dichlorbenzene: 700; methylated naphthalene: 460; xylene: 670; refined kerosene: 140; mineral oil: 83; olive oil (at 37°C): 45; stable in water emulsions to 90%; rather more resistant than DDT to the action of alkalis, by which it is dehydrochlorinated to form 2,2-bis-(p-fluorophenyl)-1,1-dichloroethylene.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50} ca.	1120		1951
"Mammals"	or	LD_{50}	900	Given in olive oil.	129

a) Approximately 0.22 times as toxic for the mouse as DDT. 3203
b) Reported to be the least toxic of the DDT analogues tested against some fishes: *Carassius auratus*; *Gambusia* sp. 2396

2) Chronic toxicity for higher animals:
a) No data available, save that exposure to DFDT results in accumulation in the peri-renal fat. 129

3) Phytotoxicity:
a) Slight phytotoxicity has been demonstrated for sweet corn (*Zea mays*). 353,129

4) Toxicity for insects:
a) Comparison of toxicities for certain insects of p,p'-DDT and its p,p' bromine and fluorine analogues. Modified from 2231.

Insecticide	I*(LC_{50}, %)	II* (LC_{50},%)	III*(LC_{50}, relative)	IV*(LC_{50}, relative)	V*(LC_{50} ppm)	VI*(LC_{50}, %)	VII* (LC_{50}(μg/g)
DFDT	1.4	5	1.01	4.4	.007	.006	5.0
DDT	0.3	0.53	1.0	1.0	.002	.001	1.65
p,p' Br analogue	0.6	1.4	1.6	1.1	.0025	.06	1.95

*I=*Pediculus humanus*, II=*Cimex lectularius*, III=*Macrosiphoniella sanborni*, IV=*Oryzaephilus surinamensis*, V=*Anopheles quadrimaculatus* (larva) VI=*Heliothrips haemorrhoidalis*, VII=*Musca domestica*.

b) The order of toxicity for *Drosophila melanogaster* of the DDT halogen analogues at the p,p' positions is as follows: 1933
DFDT > DDT > Bromo analogue > Iodo analogue
(1) DFDT has been reported 2.5 times as toxic for *Drosophila* as p,p'-DDT. 1816

c) Reported to be more toxic than DDT for *Blattella germanica*, *Oncopeltus fasciatus*, *Tribolium confusum*, 2229
all of which are relatively resistant to DDT. 353

d) Reported as less toxic than p,p'DDT, or its p,p' bromine analogue, as a larvicide for *Anopheles*. 766

e) For 16 of 21 species of insects, DFDT has been reported not to be as toxic as p,p'-DDT. 299,419
2229,2396

f) Comparative toxicity of DFDT and other insecticides, used as contact sprays vs. *Pediculus humanus* 414,418
corporis and *Cimex lectularius* in white oil solutions; sprayed at a rate to give a deposit of 0.36 mg 419
solution/cm^2:

Insecticide	LC_{50} (As % Concentration) for	
	Cimex lectularius	*Pediculus humanus*
DFDT	5.0	1.4
Lindane	0.05	0.02
p-Chlorophenyl-chloromethyl sulfone	0.2	0.1
DDT	0.5	0.3
Methoxychlor	0.5	0.9
DDD	1.2	0.9
Lethane 384	—	1.5
Lauryl thiocyanate	—	5.0
Lethane 60	—	8.1

g) Comparison of DFDT and certain other insecticides in the field control of *Pyrausta nubilalis* on sweet 675
corn (*Zea mays*) ears:

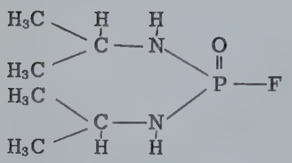
Insecticide	Lbs/100 Gals.	% Reduction Of Pyrausta By	
		Direct Action	Residual Action
DFDT	1.0	64	73
EPN	0.75	57	79
Heptachlor	1.0	70	77
Aldrin	0.75	70	74
Dieldrin	0.5	78	49
DDT	1.0	54	40
Parathion	0.5	65	18

h) Extensive data from screening tests of DFDT may be found in Ref. 1801.

20

BIS-(MONOISOPROPYLAMINO)-FLUOROPHOSPHINE OXIDE

(Isopestox®; Mipafox®; Pestox XV; Bis-(monoisopropylamino) fluorophosphate; Phosphorodi (isopropylamidic)-fluoride; N,N´-Di-isopropylphosphorodiamidic fluoride.)



Molecular weight 182.224

GENERAL **(Also consult the section on Organic Phosphates)**
[Refs.: 714,2231,2120,129,2651,87,59,713,241,2892,237,2942]

An effective systemic insecticide and acaricide, this compound was brought forward in 1951, placed on the market, but later withdrawn as suspect in the near-fatality of two workmen formulators. The two near-victims experienced a flaccid paralysis resembling that due to "ginger-jake" (tri-orthocresyl phosphate, TOCP) poisoning. This substance is closely related to bis-(dimethylamino)-fluorophosphine oxide (Hanane; BFPO) q.v., which, despite high mammalian and human hazard, finds important use as a systemic insecticide in tropical agriculture, especially in the protection of the cacao tree from certain mealy-bugs.

PHYSICAL, CHEMICAL [Refs.: 2651,2231,2120,129]

A white, odorless, tasteless, crystalline solid; m.p. 60°C; b.p. 125°C at 2 mmHg; $d_{4^\circ}^{25^\circ}$ 1.2; v.p. 0.001 mmHg at 5°C; soluble in water to about 8% at ordinary temperatures; soluble in polar organic solvents and slightly soluble in petroleum oils; slightly hygroscopic; non-corrosive; indefinitely stable as dry crystals or in solution in dry esters; slowly decomposed by water and more rapidly by acids, alkalis and plant enzymes; half-life at pH 4=14 days, at pH 5=80 days, at pH 6=200 days, at pH 7=60 days, at pH 8=6 days.

Formulations: Formulated for experimental use as an anhydrous solution (50% active agent) with a wetting compound. Applied ordinarily as a spray at 0.5%-1.0% active ingredient.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mammals	or	LD_{50}	25- 50	Severe neurotoxic signs.	2651
Rat	ip	LD_{50}	25- 50	"	2651
Rabbit	or	LD_{50}	80-100		129,2120
Guinea Pig	or	LD_{50}	80-100		129,2120

2) Pharmacological, pharmacodynamic and other effects:
- a) Sub-lethal to near lethal dosages yield severe and deleterious neurotoxic effects. 2651,190,713
  - (1) In chickens, following sub-lethal exposure, paralysis and prolonged muscular weakness have been reported.
- b) Acts as a potent inhibitor *in vitro* and evidently *in vivo* of mammalian choline esterase(s). 713,714
  - (1) Shows marked affinity for mammalian pseudo-choline esterase(s).
- c) Male and female rats differ in sensitivity to Isopestox®, the male being the more sensitive sex. 713
- d) In chickens has been shown to cause demyelinization of nerves, a property shown also by two other selective inhibitors of pseudo-choline esterase(s), tri-o-cresyl phosphate and diisopropyl phosphofluoridate. 713 713 720
  - (1) Poisoned birds showed a flaccid paralysis characteristic also of certain human poisonings.
- e) Isopestox® intoxications in man: 237,713
  - (1) The subjects were three factory workers preparing Isopestox® on a pilot plant scale.
  - (2) Toxic symptoms included: Muscular weakness (the striking feature in all three cases); gastrointestinal signs (in the more severely affected patients); bronchospasm and abnormal sweating (in the less seriously affected patient); pupillary constriction (in all cases).
  - (3) Central nervous system signs were few in all instances but two victims developed flaccid paralysis of all limbs with the paralysis being of slow onset in the third week after the phase of acute symptoms. This paralysis resembled that which follows tri-o-cresyl phosphate, also a potent inhibitor of choline esterase(s) *in vivo* and *in vitro*.
  - (4) The subjects showed decline in both the specific and the pseudo-esterases.
  - (5) The delayed signs shown by human subjects and experimentally elicited from chickens, warn against categorical assumptions that no sequelae attend these types of poisoning, particularly in cases of repeated exposure, if the acute effects can be mastered.
  - (6) Atropine is specific vs. the muscarinic but not vs. the nicotinic effects.
- f) In chickens subjected to Isopestox® at dosages of 1 mg/k by mouth or intravenously, the acute signs lasted 1 or 2 days, but the delayed effect did not develop for 10 to 14 days. The acute signs were controlled by atropine. 713 190
- g) Rats which received 300 ppm Isopestox® in the ration for 3 months exposure revealed fine muscle twitching and weakness in slope-climbing tests. Brain and heart choline esterase(s) declined to 5% to 10% of normal. 190
- h) Rabbits, fed 300 ppm in the ration, showed general weakness and head-drop in 2 to 4 weeks with the onset time being variable. Signs disappeared after returning the animals to normal rations. 190

3) Phytotoxicity:
- a) The use of Isopestox® as a systemic insecticide, both as a spray and by soil implantation in capsules, suggests that at dosages insecticidally effective the phytotoxic hazard is not high. 2651

4) Toxicity for insects and acarines:
- a) Reported results on Isopestox® effectiveness in pest control: 2651

Plant	Pest	Type Test	Conc. (%)	Applied As	Result	Country
Apple	*Aphis pomi*	Field	.05	Leaf Spray	100% kill	Austria
"	*Aspidiotus perniciosus*	Laboratory	.2	"	88% "	U.K.
Peach	*Hyalopterus arundinis*	Field	.05	"	100% "	"
Gooseberry	*Tetranychus telarius*	Greenhouse	.05	"	98% "	"
Citrus	*Tetranychus bimaculatus*	Laboratory	.05	"	100% "	"
"	*Icerya purchasi*	Field	.05	"	Good control	Italy
"	*Toxoptera aurantii*	Field	.05	"	"	"

a) Reported results on Isopestox® effectiveness in pest control: 2651

Plant	Pest	Type Test	Conc. (%)	Applied As	Result	Country
Citrus	Saissetia oleae	Field	.05	Leaf Spray	Good Control	Italy
Vicia faba	Aphis fabae	"	.1	"	97% kill	U.K.
Brussels Sprout	Brevicoryne brassicae	"	.1	"	95% "	"
Peas	Frankliniella robusta	Greenhouse	.2	"	97% "	"
Potato	Aphids	Field	.1	"	95% "	"
Hops	Phorodon humuli	"	.05	"	99% "	"
Tobacco	Myzus persicae	"	.15	"	98% "	Italy
Sugar Beet	"	"	.1	"	99% "	U.K.
"	Aphis fabae	"	.1	"	99% "	U.K.
Asters	Aphids	"	.1	"	100% "	"
Carnation	Tetranychus telarius	Greenhouse	.1	"	100% "	"
Carnation	Tetranychus telarius	Greenhouse	.1	Soil Treatment	100% "	U.K.
Chrysanthemum	Macrosiphoniella sanborni	"	.07	Leaf Spray	100% "	"
"	"	"	.22	Soil Treatment	100% "	"
Dahlia	Aphis fabae	Field	.05	Leaf Spray	100% "	"
Chrysanthemum	Phytomyza atricornis	Laboratory	.025	Soil Treatment	Young larvae killed	
Lonicera	Hydaphis xylostei	Field	.025	Leaf Spray	100% kill	U.K.
Hydrangea	Tetranychus telarius	Greenhouse	.025	"	100% "	"
Lilium	Myzus circumflexus	"	.1	"	100% "	"
Primula	Pemphigus auriculae	"	.1	Soil Treatment	100% "	"
Rosa	Macrosiphum rosae	Field	.1	Leaf Spray	100% "	"
Sweet Pea	Macrosiphum pisi	"	.1	Solution Culture	100% "	"

b) Isopestox® and other insecticides vs. Tetranychus telarius on Hydrangea. Systemic action: 1267

Compound	Method	Concentration (%)	Kill (%)
Isopestox®	Soil Soak	0.05	99
Schradan (OMPA)	Soil Soak	.1	56
Isopestox®	Spray	.05	98.5
Schradan (OMPA)	Spray	.1	75.5

c) Isopestox® vs. beneficial insects:

(1) Mortality of Brevicoryne brassicae (cabbage aphid) and its predators exposed to spray dosages of 2 cc/plant of a 0.4% concentration of Isopestox® : 2651

Insect	Mortality (%) After				
	24 hrs	10 days	20 days	30 days	40 days
Brevicoryne brassicae	100	57	19	9	5
Coccinella septempunctata	100	4	0	0	0
Syrphid larvae	100	0	0	0	0
Aphidius brassicae	100	0	0	0	0

(2) Mortality of Brevicoryne brassicae, its parasite Aphidius brassicae and its predators Syrpha spp. and Coccinella septempunctata exposed on plants treated with Isopestox® via soil soaks at concentrations of 0.4%: 2651

Dosage/Plant (cc)	Insect	Mortality (%) After				
		24 hrs	10 days	20 days	30 days	40 days
2	Brevicoryne brassicae	60	71	32	11	0
5	" "	83	79	41	17	5
10	" "	93	94	52	11	8
10	Aphidius brassicae	0	0	1	0	0
10	Coccinella septempunctata	0	0	1	0	0
10	Syrpha spp. (larvae)	0	1	0	5	0

21

BORAX (Sodium tetraborate; Sodium biborate; Sodium pyroborate.)

$Na_2B_4O_7 \cdot 10H_2O$ Molecular weight: 381.43

GENERAL

[Refs.: 2120, 129, 353, 1633, 2029, 2815, 1059, 757, 2984, 1274]

As an insecticide, borax has limited uses against ants, silverfish, Musca domestica larvae in dung heaps and chicken houses. Has known long use as a mild antiseptic and fungicide. Has shown distinct value as an herbicide, under appropriate conditions. Its fungicidal activity has been used in preventing mold on citrus. Borax has also been used in mixtures, for example, with sodium chlorate, to reduce fire hazard, as 9 parts borax to 1 part sodium chlorate for soil sterilization. Has also been used as a dust in the control of cockroaches.

PHYSICAL, CHEMICAL

[Refs.: 2221, 2120, 129, 353, 2815, 1059]

A colorless crystalline solid, or a white, granular, or crystalline powder; m.p. 75°C; $d_4^{20°}$ 1.73; soluble in water to 1g/16cc at 10°C, 1g/0.6cc at 100°C; insoluble in alcohol; soluble in glycerol to the extent of 1g/1 cc; water solutions are alkaline in reaction; incompatible with acids and with alkaloidal and metallic salts; efflorescent in warm, dry air.

Formulations: In dry mixtures, or neat, for use as a dust, powder or spray. Should be kept in tight containers.

TOXICOLOGICAL

1) Acute toxicity for mammals is low.
   - a) 15-30 g may be fatal to man (adult).
   - b) In the chronic intoxication known as "borism", there are manifestations of gastric irritation and skin eruptions. 2221,1221
   - c) Values for the acute toxicity of boric acid may be suggestive:

Animal	Route	Dose	Dosage (mg/k)	
Mouse	or	LD_{50}	3450 ± 158	2495
Mouse	sc	LD_{50}	1740 ± 130	2495
Mouse	sc	LD_{50}	2070 ± 170	2495
Mouse	iv	LD_{50}	1780 ± 121	2495
Rat	or	LD_{50}	5140	2907
Rat	or	LD_{50}	2660 ± 220	2495
Rat	iv	LD_{50}	1330 ± 112	2495
Guinea Pig	sc	LD_{50}	1200 ± 80	2495
Dog	or	LD_{50}	>1000	1036

     - (1) 15-20 g has been estimated as fatal to adult man; 5-6 g fatal to infants. 2495
     - (2) Experimental animals show no symptoms with daily intake of moderate amounts. 1069
     - (3) Sufficient amounts of borax depress the heart and spinal centers. 129
   - d) Boron, in concentrations to 30 ppm (as the element) is not harmful in drinking water 1230, 93, 2400
     - (1) A limit of 20 ppm (as the element) has been recommended. 1590
   - e) Contamination of food with borax should be guarded against and it should be kept from children and domestic animals. 129

2) Toxicity for certain aquatic invertebrates:
   - a) The threshold concentration for immobilization of Daphnia magna is ca 120 ppm, and is much less than 240 ppm. 68, 2400
   - b) The toxic threshold concentration for the flatworm, Polycelis nigra, is 1530 ppm., as borate ion. 1727

3) Phytotoxicity:
   - a) The phytotoxic potential for all vegetation is high. 129
     - (1) Borax has been used as a weed-killing herbicide, for example, against Hypericum sp. (St. John's wort) and against poison ivy. 2029, 2984
     - (2) Boron (as the element) in concentrations in water above 2-5 ppm may injure most plants; 0.5 ppm may be injurious to many plants. 2793, 1767

4) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Musca domestica (larva)	medium	LC_{50}	2000 ppm	Although at 924 ppm larvae may not be killed this concentration prevents the emergence as adults of 50% of the expected flies.	2179 2180

4) Toxicity for insects:

Insect		Route	Dose	Dosage	Remarks	
Musca domestica (larva)		medium	LC_{100}	0.224% w/w		2179
Musca domestica (larva)		medium	LC_{80}	0.112% w/w		2179
Musca domestica (larva)		medium	LC_0	0.050% w/w		2179
Periplaneta americana	(adult)♂	contact	LD_0	= .9 mg/g	LD_{50} = 2.5 mg/g LD_{100} = 4.0 mg/g	2219
P. americana	(adult)♀	contact	LD_0	= 2.5 mg/g (nontoxic)		2219
P. americana	(adult)♂	or	LD_0	= 1.4 mg/g (nontoxic) = 4.5 mg/g	LD_{100} = 12.0 mg/g	2219
P. americana	(adult)♀	or	LD_0	= 2.0 mg/g (nontoxic) = 8.0 mg/g	LD_{100} = 16.0 mg/g	2219
P. americana	(adult)♂	inj	LD_0	= 1.8 mg/g (nontoxic) = 2.1 mg/g	LD_{100} = 2.4 mg/g	2219
P. americana	(adult)♀	inj	LD_0	= 1.8 mg/g (nontoxic) = 2.6 mg/g	LD_{100} = 3.6 mg/g	2219

a) Borax is less toxic for Musca domestica larvae in the food medium than either thiourea or phthalonitrile. 2179

Concentration in medium (%)	Mortality *(%) With		
	Thiourea	Phthalonitrile	Borax
0.224	—	—	100
0.112	100	100	81
0.050	99	68	0
0.028	96	53	—
0.014	86	0	—
0.007	9	—	—

*Judged by the number of imagines finally emerging.

b) In control of Musca, borax may be applied to known breeding places such as manure piles, privies, refuse. Being water soluble it may be applied to the surface whence it diffuses into the mass to be protected. 353

c) Used as a dust to control cockroaches, borax accumulates on the ventral surfaces and coxae of the insect. 2750
   (1) It enters the body by penetrating the cuticle, and is also ingested in the grooming process. However, even though grooming is prevented, a sufficient amount enters by the integument to cause death in 2-10 days for Periplaneta and Blatta. 2750

d) Pharmacological action vs. insects:
   (1) Exposed to borax dusts, Periplaneta and Blattella show uneasiness and increased irritability followed by torpor, broken by nervous spasms, with paralysis and death ensuing in 4-48 hours after exposure. 2750 353

22

BUTOXY POLYPROPYLENE GLYCOLS 400 AND 800 (Crag Fly Repellent; Experimental Miticide 7.)

$C_4H_9[OCH(CH_3)CH_2]_nOC_4H_9$

GENERAL

Introduced as repellents for such biting flies of livestock as Stomoxys calcitrans, Siphona irritans, Tabanus spp., and for houseflies, black flies and midges. Have been used as experimental acaricides on non-food crops, at concentrations of 1 1/2 parts per 100 gallons. There is evidence suggesting a synergistic action with pyrethrins. Will be referred to below as "BPG" 400 or 800. 1246

PHYSICAL, CHEMICAL

Colorless liquids whose boiling point and viscosity depend on the mean molecular weight; $d^{25°}_{4°}$ "BPG" 400:0.973, "BPG" 800:0.990; v.p. "BPG" 400: 1×10^{-2} mm$^{30°}$C, "BPG" 800: 1×10^{-3} mm$^{30°}$C; very slightly soluble in water; "BPG" 400: 0.2g/100 g at 20°C; "BPG" 800: 0.1 g/100 g at 20°C; aqueous solutions may be prepared by using non-ionic emulsifying agents; soluble in acetone, ethanol and many organic solvents; miscible with chlordane; dissolves 18% DDT by weight and 100% toxaphene by weight; a solvent also for methoxychlor, DDD, Derris extracts and lindane; compatible with the oil carriers used in fly sprays; flash point: "BPG" 400 = 375°F, "BPG"800 =420°F. 1246

TOXICOLOGICAL

1) Of low toxicity for mammals and without skin penetration hazard. 1246
   a) No irritation reported from contact with human skin.
   b) No dermatitic symptoms in livestock from "BPG" 400 or 800 applied to cattle at strengths to 25% in non-toxic oil.

2) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage	Remarks	
Rat	or	LD_{50}	9.1 g/k		1246
Rabbit	or	LD_{50}	23.9 g/k		1246
Rabbit	ct	MLD(ca)	20 cc/k	As single dose; 1/10 died.	1246

3) Chronic toxicity:

a) In rabbits, daily cutaneous inunction of 1g/k for 90 days produced no injury save a transient erythema and desquamation. 1246

b) In rats, feeding of 0.62 g/k for 90 days produced no apparent injury. 479

4) Toxicity and repellency for insects:

a) General:

(1) Formulations with 5-10% "BPG" 800 are highly effective on the day of treatment, repelling *Stomoxys calcitrans*, *Siphona irritans*, *Tabanus* spp, *Musca domestica*, from cattle. 1247

(a) Protection declines sharply by second day.

(b) The base oil used has a marked effect on resulting repellency.

(c) Selection may be made of an oil which interferes least with repellency characteristics of "BPG" *per se* and such oils may be used which enhance effectiveness to the maximum for practical use.

(d) Emulsions of "BPG" seem to be as effective as oil base sprays; the inclusion of certain sticking agents does not enhance repellency.

(2) Sprays, possessing insecticidal as well as repellent properties, are formulated by combining organic thiocyanates, pyrethrins and allethrin with 5-10% "BPG" preparations. 2120

b) Comparative repellency tests by the "half cow method" with butoxy propylene glycols and certain other repellents. Insects chiefly *Stomoxys calcitrans* and *Siphona irritans*: 1246

Repellent	Spray Concentration (%)	—% Repellency At— 2 hrs.	4 hrs.	6 hrs.	Total Repellency (%)
Butoxy propylene glycol 800	20	73-90	70-100	67-86	77-86
Butoxy propylene glycol 800	5	82	93	87	88
n-Butyl mesityl oxide oxalate	20	88	62	0	58
Iso-bornyl thiocyanoacetate	20	0-66	60-70	60-78	51-72
Iso-bornyl thiocyanoacetate	5	50	66	74	60
Base oil		7	17	26	18

		Average % Repellency At						
		2 hrs.	3 hrs.	4 hrs.	5 hrs.	6 hrs.	7 hrs.	
Butoxy propylene glycol 800 (in oil)	10	83	54	61	66	40	60	58
Butoxy propylene glycol 800 (in H_2O)	10	38	75	40	32	34	65	48
Butoxy propylene glycol 400 (in H_2O)	10	42	94	68	72	78	81	73
Butoxy propylene glycol 400 (in oil)	10	67	60	40	24	19	89	49
Iso-bornyl thiocyanoacetate (in oil)	10	61	76	44	62	18	90	57
Base oil	10	10	26	13	30	23	12	19

c) Butoxy polypropylene glycol 800 as a pyrethrin activator in Peet-Grady tests vs. *Musca domestica*: 1246

Pyrethrins (mg/100 cc)	% Activator † in Deobase oil	% *KD 10 min.	% Mortality 24 hrs.	**OTI Difference
100 (OTI**)	0	98.3	57.5	—
50	2.5	98.1	59.8	+2
50	5.0	98.5	65.8	+8
50	10.0	96.9	78.7	+21
60	10.0	98.8	84.1	+26
40	10.0	97.2	65.1	+7
30	10.0	97.2	67.6	+10
0	10.0	59.7	37.6	-22
6.25	10.0	79.7	41.8	—
6.25	5.0	86.0	47.9	—
6.25	2.5	76.6	41.6	—
		Butoxy polypropylene glycol 400		
6.25	10.0	92.5	51.5	—
6.25	5.0	78.4	40	—
6.25	2.5	79.8	39.5	—
6.25	0	45.5	8.7	—
100 (OTI**)	0	97.6	47.8	—

* KD = "Knock Down".

** OTI = Official Test Insecticide.

† Activator: Butoxy polypropylene glycol 800.

23

2-BUTOXY-2′-THIOCYANODIETHYL ETHER (β-Butoxy-β′-thiocyanodiethyl ether; 2-[2-(Butoxy) ethoxy] ethyl ether of thiocyanic acid; Butyl carbitol rhodanate; Butyl carbitol thiocyanate; Lethane 384®.)

$C_4H_9OCH_2CH_2OCH_2CH_2SCN$ Molecular weight 203.3

GENERAL

[Refs: 2331, 130, 353, 2231, 2815, 1059, 757, 1430, 1236, 2352, 414, 2124 669, 2294, 3060, 636, 2533, 444]

1) An insecticide belonging to the general class of organic thiocyanates, (see the general treatment of). This class of compounds has been extensively tested for insecticidal and acaricidal activity.
   a) Several members of the group have been brought out as practical insecticides under the designation of "Lethanes", for example,
      (1) Lethane 384® (the present compound),
      (2) Lethane 60®, q.v. which is β-thiocyanoethyl laurate, the principal ingredient of an ester mixture,
      (3) Lethane A-70, a 90% solution of β, β′ dithiocyanoethyl ether, Lethane B-71a and Lethane B-72, which are, respectively, a 13.5% dust and a wettable powder of the same strength.
      (4) Lethane 384® Special is a mixture of Lethane 384®, 12.5%, + Lethane 60®, 37.5%, in 50% petroleum oil.

2) The term "Lethanes" meant originally the alkyl thiocyanates but now includes compounds derived from the thiocyanation of the alkyl groups of ethers, or the alkyl or acyl groups of esters. Thus, for example, lauryl thiocyanate is "generically" speaking, a "Lethane".

3) The alkyl thiocyanoacetates, characterized by rapid "KD" or "knock down" activity, have been developed as contact insecticides. Alkyl thiocyanates, relatively, have poor "KD" potential.
   a) The α-thiocyanoketones have the most rapid "KD" action, this activity being at its maximum at a chain length of C_9.

4) Among the lower alkyl thiocyanates, R-S-C≡N, are excellent, but phytotoxic, fumigants, e.g. methyl and ethyl thiocyanate, which are highly effective toxicants for *Aonidiella*, *Sitophilus oryzae* and *S. granarius*.
   a) n-Octyl thiocyanate has a high contact toxicity for *Pediculus*; the octyl, decyl, lauryl thiocyanates are toxic for *Cimex* (LC_{50} = a 5% spray) with the peak of toxicity at lauryl. Increasing chain length (beyond lauryl) is marked by decline in toxicity.
      (1) Lauryl thiocyanate is effective against aphids and red spider mites (eggs included).

5) Among the isothiocyanates, R-N=C=S, with alkyl substitution on N rather than S, are substances potent against such scale insects as *Aonidiella*.
   a) Ethyl isothiocyanate is a fine soil fumigant for *Limonius*, being 100 times more potent than ethyl thiocyanate.
   b) Allyl isothiocyanate is said to be outstanding in activity against *Musca domestica*, *Agriotes*, *Sitophilus*, *Tribolium*.

6) In general, these compounds bring on a quick narcosis of insects.

7) The "lethane thiocyanates" are effective as dusts against the pea aphid, *Macrosiphon onobrychis* (= *Illinoia pisi*), house flies, clothes moths.

8) Lethane 384®, 2-butoxy-2′-thiocyanodiethyl ether, like other thiocyanates of its class, exhibits marked contact toxicity for many insects, aphids in particular. "Knock down" effect on flies and mosquitoes is very rapid, and it has proved an excellent insecticide in household space sprays and in livestock sprays in combination with, or as substitute for, pyrethrins. It has a marked toxicity for the winter eggs of aphids.

9) Also see the general treatment Miticides or Acaricides.

PHYSICAL, CHEMICAL

A yellow to brown, oily liquid; b.p. 124°C at 0.25 mmHg; $d_{4^\circ}^{25^\circ}$ 0.915-0.93; virtually insoluble in water; soluble in most organic solvents and in petroleum oils; flash point not less than 125°F (closed cup). Lethane 384® contains 53-56% (average 54.5%) by weight, 50% by volume, of the active agent in question, 2-butoxy-2′-thiocyanodiethyl ether. To be dealt with under proper precautions. Absorbable through unbroken skin; contaminated members should be washed at once, and contaminated clothing changed. Prolonged breathing of mists is hazardous, and the eye is particularly vulnerable as a portal of entry.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Acute: (Dosages are given in terms of Lethane 384® which contains 50% v/v of the active ingredient in light petroleum oil.

Animal	Route	Dose	Dosage		Remarks	
Rat	or	LD_{50}	90	mg/k		1951
Rat	or	LD_{50}	0.5	cc/k		2078
Rat	ct	LD_{50}	0.6	cc/k	Death within 8 hours.	2078
Rat	sc	LD_{50}	0.55	cc/k		2078
Rat	ip	LD_{50}	0.09	cc/k		2078
Guinea Pig	or	LD_{50}	0.4	cc/k		2078
Guinea Pig	sc	LD_{50}	0.45	cc/k		2078
Guinea Pig	ip	LD_{50}	0.084	cc/k		2078
Rabbit	or	LD_{50}	0.12	cc/k		2078
Rabbit	ct	LD_{50}	0.4	cc/k		2078
Rabbit	ct	LD_{50}	0.25-0.5	cc/k		1951
Rabbit	sc	LD_{50}	0.1	cc/k		2078
Rabbit	ip	LD_{50}	0.08	cc/k		2078
Dog	or	LD_{50}	0.05	cc/k		2078
Dog	sc	LD_{50}	0.2	cc/k		2078

(1) Acute toxicity of Lethane 384® Special, which consists of 3 parts of Lethane 60® to 1 part Lethane 384®:

Animal	Route	Dose	Dosage mg/k	
Rat	or	LD_{50}	400	1951
Rabbit	ct	LD_{50}	1000	1952

   b) Chronic toxicity:
      (1) 4% Lethane 384® is said to have been fed to rats for 4 years with no ill effects. 129
      (2) Single, 500 mg/k doses, and 125 mg/k multiple doses, constitute a high hazard to man. 3201, 1951, 1859

2) Pharmacology, symptomatology, physiological action etc:
   a) Toxicity of the alkyl thiocyanates increases in descending series to methyl thiocyanate, (acute LD_{50} for rat, oral = 60 mg/k). 3201, 1951, 1859
      (1) Subcutaneous doses are 300-600 times as toxic as oral doses.
      (2) Lower analogues are characterized by rapid toxic action.
      (3) Lethanes and higher alkyl thiocyanates are skin irritants.
   b) Symptoms: Organic thiocyanate intoxication: Sequence:
      (1) Restlessness, irritation; (2) depression; (3) cyanosis; (4) dyspnoea; (5) tonic convulsions; (6) death in 1951
      respiratory paralysis, occurring swiftly after reception of the lethal dose. 2078
   c) Organic thiocyanates are paralytic, but not narcotic, central nervous system toxicants and asphyxiate on inhalation of vapors. 3062
      (1) Postulated by some that they release HCN, with consequent cyanide intoxication effect.
      (2) The higher homologues produce liver, and other organ, damage, this being general with Lethane 384®. 1951
      Vacuolation of liver and a pneumonitis of a fibrinous, monocytic type has been noted. 2078
      (3) It is assumed that sub-lethal doses can be excreted, thiocyanate (-SCN), at 3 mg per day, being a regular urine component. 353

3) Phytotoxicity:
   a) A certain phytotoxic hazard suggests use on plants principally when these are dormant or in the early stage of bud development. 2120
   b) Toxicity to certain ornamental plants of a combination of 2-butoxy-2′ - thiocyanodiethyl ether and oil, of which a 1 1/2% dilution contained 0.0713% 2-butoxy-2′ -thiocyanodiethyl ether and 0.0937% petroleum oil. Concentrations are in terms of this combination: 638

Plant	Concentration of Concentrate (%)	Concentration of Spreader (%)	Temperature (°F)	Relative Humidity (%)	Result (Injury)
Cherry laurel	1.5	0	93	72	Injury.
Cherry laurel	2.5	0	93	72	50% damage; tip, margin burn.
Cherry laurel	3.0	0	93	72	Complete destruction; leaf drop in 1 week.
Ligustrum	1.5	0	93	72	No injury.
Ligustrum	2.5	0	93	72	No injury.
Ligustrum	3.0	0	93	72	Slight, marginal burn.
Ligustrum	1:400	1:400	90	66	Marginal burn, tip to petiole.
Ligustrum	1:600	1:150	90	66	Less severe injury than preceding.
Ligustrum	1:800	1:200	90	66	Slight, marginal burn near petiole.
Ligustrum	1:1000	1:250	90	66	No injury.

b) Toxicity to certain ornamental plants of a combination of 2-butoxy-2'-thiocyanodiethyl ether and oil, of which a 1 1/2% dilution contained 0.0713% 2-butoxy-2'-thiocyanodiethyl ether and o.0937% petroleum oil. Concentrations are in terms of this combination:

Plant	Concentration of Concentrate (%)	Concentration of Spreader (%)	Temperature (° F)	Relative Humidity (%)	Result (Injury)
Croton	1:100-1:800	1:100-1:250	80-82	86-90	No injury.
Chrysanthemum	1:1000	1:250	100	57	Leaves scorched.
Chrysanthemum	1:1200	1:300	100	57	Heavy tip, marginal burning.
Chrysanthemum	1:1400	1:350	100	57	Moderate tip, marginal burning.
Chrysanthemum	1:1800	1:450	100	57	No injury.
Chrysanthemum	1:1000*	1:250	100	57	No injury.
Viburnum	1:400-1:800	1:100-1:200	89	68	No injury.
Pitosporum	1:400-1:800	1:100-1:200	82	90	No injury.
Feijoa	1:400-1:600	1:100-1:150	82	90	Complete leaf destruction.
Feijoa	1:800	1:200	82	90	Slight tip, marginal injury.
Feijoa	1:1000	1:250	82	90	No injury.

*Rinsed off after 15 minutes.

(1) Other bibliography on phytotoxicity, etc. [2329, 2331, 2330, 2353, 2620, 2966]

(2) As Lethane 410®, a commercial insecticide, there was no foliage or blossom damage to wide variety of plants. 2329

(3) Harmless to carnations when used as an acaricide in 0.25% emulsion. 2331

(4) Other organic thiocyanates, e.g. p-thiocyanoaniline, are markedly phytotoxic. p-Thiocyanoaniline seriously damages Nasturtium. 1430

4) Toxicity to insects:

Insect	Route	LD_0	LD_{50} (mg/g)	LD_{100}	Remarks	
Oncopeltus fasciatus	Contact (as Lethane 384)	0.12	0.40	0.75	Av. wgt. of insects .065 (.04-.09) g.	2219
Periplaneta americana ♂	Contact "	0.36	0.66	1.36	Av. wgt. of insects 0.9 (.7-1.15) g.	2219
Periplaneta americana ♂	inj "	0.1	0.15	0.2	Av. wgt. of insects 0.9 (.7-1.15) g.	2219
Periplaneta americana ♀	Contact "	0.56	1.26	2.3	Av. wgt. of insects 1.3 (1.0-1.9) g.	2219
Periplaneta americana ♀	inj "	0.12	0.2	0.4	Av. wgt. of insects 1.3 (1.0-1.9) g.	2219
Popillia japonica	Contact "	0.35	0.8	1.7	Av. wgt. of insects .096 (.07-.14) g.	2219
Popillia japonica	inj "	0.1	0.3	0.9	Av. wgt. of insects .096 (.07-.14) g.	2219
Tenebrio molitor	Contact "	0.4	0.85	1.6	Av. wgt. of insects .105 (.08-.15) g.	2219
Pediculus humanus	Contact Spray		LC_{50} = 13.5 µg/g			413
Cimex lectularius	Contact Spary		LC_{50} = 450 µg/g			413

a) Comparative toxicity of 2-butoxy-2'thiocyanodiethyl ether, as Lethane 384® and other insecticides for Pediculus humanus and Cimex lectularius as direct sprays in refined white oil (P31); concentration varied (solvent volume constant) sprayed at 0.36 mg/cm² at which rate the oil carrier is harmless. In some instances, as indicated, aqueous preparations as solutions or suspensions were employed and sprayed at the rate of 1.8 mg liquid/cm². Also, as indicated, dusts were employed either neat or as kaolin dilutions: 424, 418 432

(1) Spray tests, in P31 oil, at 0.36 mg/cm²; LC_{50} given as % concentration. Average number exposed per trial: Lice—40, bed bugs—30. Comparison Lethane 384 and others:

Pediculus humanus

Insecticide	LC_{50}(%)
Lethane 384®	1.5
Lethane 384 Special	2.4
Lindane (γ-BHC)	0.016
DDT	0.030
Pyrethrins (+2% isobutyl undecyleneamide)	0.038
Pyrethrins	0.47
Thanite (isobornyl thiocyanoacetate)	3.2
Lauryl (dodecyl) thiocyanate	6.0
Bis-ethyl xanthogen	6.2
Lethane 60®	8.1
Benzyl benzoate	21.0

Cimex lectularius

Insecticide	LC_{50} (%)
Lethane 384®	4.0
Lethane 384 Special	12.5
Pyrethrins + (2% isobutyl undecyleneamide)	0.026
Pyrethrins	0.045
Lindane (γ-BHC)	0.051
DDT	0.56
Lauryl (dodecyl) thiocyanate	19.5
Lethane 60	32
Thanite	75
Bis-ethyl xanthogen	75
Benzyl benzoate	75

(2)

Insecticide	LD_{50} (Contact Spray) µg/insect,		mg/k	
	lice	bug	lice	bug
Lethane 384®	.27	1.8	135	450
Lindane	.003	.023	1.5	6
Pyrethrins	.085	.02	42	5
Pyrethrins (+2% isobutyl undecyleneamide)	.007	.012	3.5	3
DDT	.054	.25	27	63

(3) Comparison of toxicities of Lethane 384® and other thiocyanates:

Insecticide	LC_{50}(Conc. %), Direct Spray In P 31 Oil (.36 mg/cm^2)		
	Pediculus humanus	Cimex lectularius	Ratio
Lethane 384 ®	1.5	4.0	× 2.7
Lethane 384 Special®	2.4	12.5	× 5.1
Lauryl (dodecyl) thiocyanate	6.0	19.5	× 3.2
Lethane 60 ®	8.1	32.0	× 3.9

(4) Comparison of toxicities, Lethane 384 ® and others; LC_{50}, as direct spray in P 31 oil at 0.36 mg/cm^2 vs. eggs (various ages) of Pediculus humanus:

Insecticide	LC_{50} (%)
Lethane 384 ®	6
Lauryl thiocyanate	18
DDT	3 (Saturated) gave 8% kill only.
Bis-ethyl xanthogen	> 50 Gave 30% kill only.
Benzyl benzoate	> 50 Gave 40% kill only.
Thanite	> 50 Gave 15% kill only.

(5) Comparison of toxicities, for Pediculus humanus corporis, of Lethane 384 ® in direct spray tests. Insecticides in oil solution (P 31 oil) sprayed at rate of 0.36 mg/cm^2.

Compound	LC_{50} (%) For Adult Body Lice
Octyl thiocyanate	5
Decyl thiocyanate	5
Dodecyl thiocyanate	5
Tetradecyl thiocyanate	11
Hexadecyl thiocyanate	18
Octadecyl thiocyanate	25
Lethane 384 ® (2-Butoxy-2′-thiocyanodiethyl ether.)	1.5
Lethane 60 ® (Thiocyanoethyl laurate.)	8.1
Lethane 384 Special (1:3 mixture of 2 preceding.)	2.5
Lauryl thiocyanate	6
Bis-ethyl xanthogen	6.2
Benzyl benzoate	22
Pyrethrins (Commercial spray c̄ 0.44% pyrethrins.)	34
Pyrethrins (+2% isobutyl undecyleneamide: pyrethrins .04%	3

(a) In considering thiocyanates as louse insecticides, it should be kept in mind that the lower thiocyanates are especially toxic for mammals. Dodecyl (lauryl) thiocyanate may be considered a compromise between toxicity to the louse and toxicity to man.

(6) Toxicity of Lethane 384 ® and others on treated flannel. Insecticides in oil solution at various concentrations as specified. Solutions sprayed on fabrics harboring Pediculus humanus corporis:

Insecticide	Approximate LD (mg Active Ingredient/cm^2) AT		
	50% (In Oil)	10% (In Oil)	In a Volatile Solvent
Lauryl thiocyanate	0.06	0.04	0.45
Lethane 384 ®	—	0.02	—
Lethane 384 Special	—	0.02	—
Pyrethrins	0.006	0.0045	0.031

(a) Toxic effect of all treated fabrics was much reduced by washing. All treatments gave 100% kill after 7-10 days wearing, even with 3 months storage prior to wearing. Lauryl thiocyanate gave 100% kills after 11-16 days wearing at 10% in oil; at 50% in oil yielded 100% kills after 17-22 days wearing and 85% kills after 23-30 days wearing.

(b) All thiocyanates, under certain conditions, violently irritate human skin. Men, working and sweating freely in treated clothing, experience severe burning sensations and erythema. This is especially true with Lethane 384 ® and less so with Lethane 384 Special and lauryl thiocyanate. Chronic toxicity in man was not observed.

(c) Lauryl thiocyanate has been favored as a "pediculicide" since the Lethanes 384 ® and 60 ® are especially irritating to Caucasian skin.

(d) Lethane 384 Special ® is also effective vs. the head louse, Pediculus humanus capitis, but its use may entrain dermatitis.

(e) Lauryl thiocyanate and Lethane 384 ® in salves and emulsions control the human crab louse, Phthirius pubis.

(7) Field tests using 2-Butoxy-2′-thiocyanodiethyl ether against various insect pests of plants: 638

(a) Used were: (I) A commercial concentrate with 23% thiocyanate + an oil soluble emulsifier and pine oil; (II) a special concentrate, with an oil soluble emulsifier + petroleum oils of viscosity 65 seconds Saybolt:

(b) Vs. Dialeurodes citri: 2/3 of 1% thiocyanate + petroleum oil gave average kills of 80%; 1% thiocyanate gave 87.5% kills; 1 1/2% thiocyanate gave 95.1% kills; 1.5% dilution, containing 0.0713% thiocyanate + .0937% petroleum oils, proved an effective contact spray, strongly toxic to crawler stage and eggs. Most effective: Spray of 1:1600 + 1:400 spreader. On Privet (Ligustrum) 1% concentration in oil gave 69.2-98.8% kill (0.0475% thiocyanate + .0625% oil) at 83-91° F.

(c) Vs. Aphis spiraecola:

	At 82° F			
Dilution:	1:3200 + spreader 1:800	1:2400 + spreader 1:200	1:1200 + spreader 1:300	1:720 + spreader 1:180
Mortality(%)	46.0	91.5	96.6	98.3

(d) Vs. Pseudococcus citri: A spray, 1:800 + spreader 1:200 gave 57% total kill with 98.5% kill in the upper layer of insects. Application before insects have advanced to the uncontrollable "layered stage" is essential. Vs. P. citri on ornamentals, 1:1000 + spreader 1:250 gave 98.2% kill; 1:1400 + spreader 1:350 gave 81.5% kill; 1:1800 + spreader 1:450 gave 46% kill.

(e) Chrysomphalus aonidium: Aliphatic thiocyanates were not effective against the mature scale insect; valuable against crawler and first nymph stage.

(f) Eriophyes oleivorus: (Acarine): A 1:2000 dilution + spreader is toxic to this mite.

(g) Vs. aphids of ornamental plants: 1% thiocyanate + oil at 80-95° F gave 98-100% kill; 1:1000 + spreader 1:250 gave 99.4% kill; 1:1400 + 1:350 spreader gave 99.2% kill.

(8) Vs. Musca domestica as a bait in sugar or molasses:
- (a) Lethane 384® 1% in baits, used in field tests, gave: 0 mortality or knockdown in 30 minutes, in 1 hour or in 24 hours. 1915

(9) Vs. Musca domestica in space sprays: 636
- (a) Serves as supplement or replacement for pyrethrins in conferring rapid "knockdown".
- (b) Combined with DDT in 2% concentration, complete control may be had from sprays delivered by atomizers at 1cc/m³.

(10) Vs. Periplaneta americana (supplementing DDT dusts): 2792
- (a) "Knockdown" capacity is conferred on slow-acting DDT dusts by the addition of 5% of a thiocyanate such as Lethane 384®.
- (b) "Knockdown" within 1 hour may be obtained as compared with 2 days for DDT alone.

4) Pharmacological, pharmacodynamic and other biological considerations, in insects:
- a) Rapidity of "Knockdown" effect and swift onset of narcosis, is a prime characteristic of insecticidally effective thiocyanates. 1430
  - (1) 2-Butoxy-2′-thiocyanodiethyl ether possesses this effect in high measure.
- b) In Blatta, the swift onset of paralysis is not preceded by initial stimulation. 1430, 1632
  - (1) In Blattella, Lethane 60 produces brief excitement preceding paralysis with sharp decline in O_2 uptake. 1441
- c) In Periplaneta americana, the symptoms of 2-Butoxy-2′-thiocyanodiethyl ether intoxication resemble those of HCN poisoning. 588 2421
  - (1) Marked decline heart beat, giving way to a rise then leveling off; marked decrease in blood circulation.
  - (2) Lethane B71 depresses sharply the O_2 uptake of Oryzaephilus surinamensis 2041
- d) The thiocyanates are suggested as respiratory poisons. 588
  - (1) The insecticidally active thiocyanates are depressants of insect respiration, like rotenone, and in contrast to respiratory stimulants like DDT, pyrethrins, lindane, DNOC. 2041
    - (a) Acenaphthylene thiocyanate, which is non-toxic to Sitophilus granarius, shows no respiratory effect. 2999
  - (2) Metabolic release of HCN has been suggested as the cause of toxicity in mammals, but there are objections to this suggestion for insects. 3201 2231
- e) The narcotic effect in insects predominates, differing from mammals in which central nervous system paralytic effect, rather than narcotic effect, is characteristic. 3062 3107
- f) For Musca domestica there is a smaller percentage of recovery from 2-Butoxy-2′-thiocyanodiethyl ether intoxication when the treated insects are kept at a post-treatment temperature of 20°C than when they are kept at 38°C (negative temperature coefficient). 890
- g) Histopathological effects of 2-Butoxy-2′-thiocyanodiethyl ether in Musca domestica: 1422
  - (1) Dissolution of non-fibrous elements of brain cells; fibers of nerve system unaffected.
  - (2) Increase in intensity of nuclear staining.
  - (3) Dissolution of the nuclear membrane in muscle cells.

5) Acquired resistance:
- a) The DDT resistance manifested by some strains of Musca domestica exposed over a period of time to DDT is accompanied by enhanced resistance to poisoning by Lethane 384® and Lethane 384 Special® according to some reports. 259

6) In the economic control of insects: Reports of effectiveness:
- a) Ineffective vs. Lygaeus mendax. 729
- b) Inferior to DDT vs. Psallus seriatus. 331
- c) Controls (though now replaced by DDT) the jassid and cicadellid leaf hoppers. 353
- d) Inferior to DDT vs. Erythroneura comes. 518, 623, 2705
- e) May be used to control Trialeurodes vaporariorum. 2226
- f) May be used to control Macrosiphum pisi (less effective than 4% DDT in sulfur). 1910
- g) Superior, vs. Pseudococcus maritimus, to DDT, BHC, Chlordane, HETP, Toxaphene. Yielded 99% control. 2356, 1029

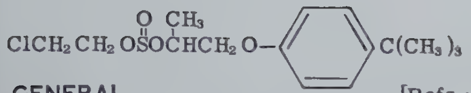
h) Cephus cinctus: Completely resistant to Lethane 384®. 1501
i) Ineffective vs. Anthonomus pomorum. 786
j) Useful, among other substances, as summer miticide vs. tetranychids. 353

7) Screen test data:
a) For results of screening test with several insects, other arthropods, consult Reference 1801.

24

BUTYLPHENOXYISOPROPYL CHLOROETHYL SULFITE

(2-(p-tert-Butylphenoxy)-isopropyl 2-chloroethyl sulfite; β-Chloroethyl-β′-(p-tert-butylphenoxy)-α-methyl ethyl sulfite; 2′-Chloroethyl-1-methyl-2-(p-tert-butylphenoxy)-ethyl-sulfite; 88 R; Aramite®; CES; Niagaramite.)



Molecular weight: 331.83

GENERAL

[Refs.: 1410, 191, 1697, 1812, 1409, 1301, 117, 1605, 2379, 2867, 129, 2120]

An acaricide of rather recent introduction which has proved itself effectively toxic to several species of phytophagous mites both in the active stages and in the egg, but low in insecticidal and phytotoxic action. It has a residual action which renders an application effective for 7 days against certain acarines. It has been effectively used as a contact acaricide at the rate of 1 lb per 100 gallons, or at 2 lbs per 100 gallons if a longer residual action is needed. Application must be made no later than 15 days before harvest of a food crop. Aramite® (the name in common commercial use) has proved to be one of the better specific acaricides lately brought into use. Effective against Tetranychus bimaculatus, Paratetranychus pilosus (=Metatetranychus ulmi), Aceria sheldoni, Bryobia praetiosa, and some others, including poultry mites.

a) Also consult the general treatment of Miticides or Acaricides in this work.
b) Screening test data for various insects may be found in Ref. 1801.

PHYSICAL, CHEMICAL

An organic sulfite, specifically a chloralkyl aryloxyalkyl sulfite, of the general class $R\text{-}O\overset{O}{\overset{\|}{S}}O\text{-}R'$; a yellowish, clear liquid when pure, the technical grade is a dark, amber-brown, oily liquid; m.p. <-31.7°C; b.p. (pure) 200-210°C at 7 mm Hg, (technical 175°C at 0.1 mm Hg; $d_{4^\circ}^{20^\circ}$ 1.148-1.152 (technical); $n_D^{27^\circ}$ 1.5705 (pure); insoluble in water; soluble in alcohol (and generally) in aliphatic solvents; miscible completely in aromatic solvents; solubility in petroleum oil declines with decreasing temperature; viscosity: 120-140 centipoises at 25°C; volatility: 0.6 psi at 37.8°C; flash point (ca) 350°C; hydrolysis in strongly alkaline conditions with yield of ethylene oxide, 1-p-tert-butyl phenoxy-propan-2-ol, and inorganic sulfite; in strong sunlight, decomposes with evolution of SO_2; incompatible with alkaline agents, e.g. lime, Bordeaux mixture; compatible with many crop protection agents, both insecticides and fungicides; non-corrosive, and may be used with vessels of black iron; the technical grade contains the active ingredient to at least 90%, accompanied by inert aryl sulfites, various xylenes, and propylene glycol as a stabilizer toward light and heat; half-life: In citrus peel = 7-8 days. 1302

a) Formulated as 15% wettable powders; 50-90% emulsion concentrates (25% emulsion base); 3-4% dusts in inert carriers or aerosols. 1061

TOXICOLOGICAL

1) Toxicity for higher animals: Acute:

Animal	Route	Dose	Dosage (g/k)	Remarks	
Rat	or	ca LD_{50}	6.3		1951
Rat	or	LD_{50}	3.9	Technical grade.	1410
Mouse	or	LD_{50}	2		129
Guinea Pig	or	LD_{50}	3.9	Technical grade.	1410

a) Chronic toxicity:
(1) Dogs on 500 ppm in diet (dry basis), exposure 20 weeks, showed no effect. 129, 2120
(2) Rats on 500 ppm in diet (dry basis), exposure 20 weeks, showed no effect. 129, 2120
(3) Rats on 500 ppm in diet, exposure 2 years, showed no effect on growth rate, lactation. 2231
(4) Rats: Threshold for significant effects was between 500-1580 ppm in diet. 2231
(5) Rats on 500 ppm for 32 weeks showed no tissue damage; on 1000 ppm for 32 weeks showed no gross effect but histopathological effects (as liver cell damage); 5000 ppm = lowest concentration producing grossly observable effects. 2231, 1953
(6) A 20% solution, on prolonged exposure, irritated human skin. 129

2) Phytotoxicity:

a) Generally low, or minimal, but damage to certain varieties of Pyrus has been noted. 129, 2120, 117

(1) Has been used without hazard on cotton, deciduous fruit trees (excepting certain varieties of pear), nut trees, beans, alfalfa, various citrus trees, ornamentals. Safe on greenhouse plants. 129 2867

3) Toxicity for Acarina:

a) Residual toxicity for Tetranychus bimaculatus in greenhouse tests on Phaseolus coccineus as host plant. Used as a 15% wettable powder at rate of 1.25 lbs/gal. About 800 mites examined per trial: 117

Days Elapsed Between Spraying of Plants and Infestation	% Mortality After	
	7 Days	14 Days
1	22.6	98.3
2	54.7	99.0
3	50.0	97.4
4	56.1	91.8
5	43.0	96.4
6	51.6	80.8
7	40.1	72.0
10	23.1	47.3
14	59.0	17.3
Control	3.7	5.4

(1) Effective acaricidal action for ca. 7 days; little ovicidal action with considerable numbers of new mites hatching.

b) Residues and residual action against Paratetranychus citri on lemon fruits at various post-spraying intervals. Used as spray of 15% wettable powder, 2 lbs per 100 gal., at rate of 1600 gallons per acre under Southern California conditions of late October: 1698

Days After Treatment	Residue (ppm)	% Mortality P. citri (Adult)
7	0.63	100
14	.41	100
21	.19	100
32	.11	80
64	.04	25

(1) Dosage, application method, and reinfestation with P. citri. Application at rate of 1600 gals. per acre; high pressure spray:

Dosage (lbs/acre)	Average No. Adult Mites Per 32 Leaf Sample At			
	21days	35 days	60 days	91 days
2	8.5	19.6	30.0	plots re-treated
4	2.3	9.4	15.0	plots re-treated
8	0.4	2.6	4.0	56

(Application at 200 gals. per acre by spray duster equipment:)

Dosage (lbs/acre)	41 days	63 days	88 days	104 days
1.5	16.5	86.0	Re-treated	—
3.0	6.0	62.0	Re-treated	—
3.6	7.0	8.0	101 (Re-treated)	—
6.0	0	0	0.4	1.5

(2) Effectiveness at 1600 gals.per acre, high pressure application, compared with 1.75% medium petroleum oil, vs. P. citri on lemon trees, under various seasonal conditions in Southern California. Test plots in diverse orchards, (8):

Spray Application In	Test Interval Days	Material	Dosage/100 Gals.	Av. No. Adult P. citri Per 32 Leaf Sample
May	88	Aramite	5 oz	0.6
May	88	Oil	1.75 gal.	0.4
July	73	Aramite	4 oz	36.0
July	73	Oil	1.75 gal.	4.0
October	304	Aramite	8 oz	286.0
October	304	Oil	1.75 gal.	25.0
October	304	Aramite	16 oz	32.0
July	93	Aramite	3.6 lbs/acre	3.0
July	93	Aramite	9.6 lbs/acre	1.0
July	80	Aramite	4.0 lbs/acre	36.0
October	304	Aramite	8.0 lbs/acre	90.0
October	304	Aramite	16.0 lbs/acre	22.0
	(On Orange Trees)			
March	60	Aramite	2.0 lbs/acre	30.0
March	60	Aramite	4.0 lbs/acre	15.0

Spray Application In	Test Interval Days	Material	Dosage/100 Gals.	Av. No. Adult P. citri/ 32 Leaf Sample
March	60	Aramite	8.0 lbs/acre	4.0
April	96	Aramite	2.5 lbs/acre	4.0
April	96	Aramite	5.0 lbs/acre	1.0
April	106	Aramite	5.0 lbs/acre	2.0
April	106	Aramite	10.0 lbs/acre	3.0
December	138	Aramite	2.5 lbs/acre	4.0

(3) As a semi-concentrate spray on citrus, at 200 gals. per acre vs. P. citri. Tested in 10 orange groves:

Sprayed In	Test Interval (Days)	Dosage lbs Aramite/Acre	Av. No. Adults/32 Leaf Sample
March	33	3	19
		6	2.8
May	42	3	0.3
May	32	1.5	8.3
		3	2.2
		6	1.0
May	53	4	0.3
April	60	3.6	0.5
April	70	3	0.1
March	88	3	63.0
		6	0.4
April	96	2	9.0
February	115	2.5	46.0
October	304	4	25

(a) Action against adult P. citri is slow; at low concentrations, 96 hrs of exposure to residues was required for inactivation. With post-treatment conditions favorable for mite development, dosage increases from 1.5 to 6 or 8 lbs/acre improved control.

(4) Toxicity of Aramite for Tetranychus bimaculatus: T = topical treatment, with mites then transferred to untreated leaves; R = residue treatment, untreated mites placed on treated leaves; TR = topical treatment with mites left in place on treated leaves: 904

Applied Via	Leaf	Formulation	LC$_{50}$ (g/100cc) By T	R	TR
Settling Tower	Bean	Emulsion	0.014	0.0031	0.0018
Settling Tower	Bean	Suspension	0.0380	0.0035	0.0023
Settling Tower	Avocado	Emulsion	—	0.0120	0.0089
Settling Tower	Avocado	Suspension	—	0.0140	0.0088
Sprayer	Avocado	Emulsion	0.0031	0.0015	0.0006
Sprayer	Avocado	Suspension	0.0056	0.0033	0.0020

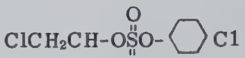
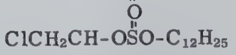
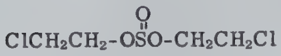
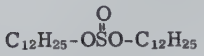
(5) Effectiveness of Aramite and parathion, as emulsions, in killing adult Tetranychus bimaculatus, placed on leaf surface opposite the treated surface: 904

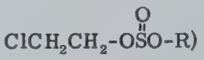
Compound	% Conc.	Leaf	Surface Treated	% Mortality (Net) At 48 Hrs.	96 Hrs.
Aramite	0.12	Bean	Upper	49.4	98.2
Aramite	0.12	Bean	Lower	82.5	100
Aramite	0.12	Grapefruit	Upper	13.1	34.2
Aramite	0.12	Grapefruit	Lower	60.8	96.1
Aramite	0.12	Avocado	Upper	0	26.0
Aramite	0.12	Avocado	Lower	0	55.3
Parathion	0.03	Bean	Upper	91.5	100
Parathion	0.03	Bean	Lower	100	100
Parathion	0.12	Grapefruit	Upper	77	100
Parathion	0.12	Grapefruit	Lower	96.7	82.5
Parathion	0.12	Avocado	Upper	52.8	100
Parathion	0.12	Avocado	Lower	85.3	98.2

(6) Effectiveness of Aramite and others vs. Tetranychus bimaculatus as residues (mites [untreated] placed on treated leaves); Settling tower application: 904

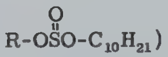
Compound	Formulation	LC$_{50}$ (g/100cc) On Bean Leaves	Avocado Leaves
Aramite	Emulsion	0.0031	0.012
Aramite	Suspension	0.0035	0.014
Parathion	Emulsion	0.0095	0.013
Parathion	Suspension	0.0072	0.0081
Sulphenone	Emulsion	0.25	0.54
Sulphenone	Suspension	0.45	0.60

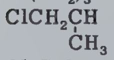
c) Organic sulfites (Aramite and related substances) structure and toxicity, measured as LD_{95} in ppm, for Tetranychus bimaculatus on infested bean plants sprayed to "run-off". Determination of mortalities at 48 hours after treatment. 1410

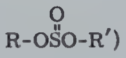
Compound	LD_{95} (ppm)
	1250
 $\mathrm{ClCH_2CH{-}O\overset{\overset{O}{\|}}{S}O{-}C_{12}H_{25}}$	150
 $\mathrm{ClCH_2CH_2{-}O\overset{\overset{O}{\|}}{S}O{-}CH_2CH_2Cl}$	5000
 $\mathrm{C_{12}H_{25}{-}O\overset{\overset{O}{\|}}{S}O{-}C_{12}H_{25}}$	10,000

(Alkyl-2-chloroethyl sulfites:  $\mathrm{ClCH_2CH_2{-}O\overset{\overset{O}{\|}}{S}O{-}R}$)

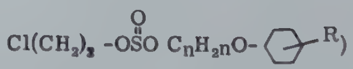
R	LD_{95} ppm
nC_4H_9	10,000
nC_7H_{15}	1,000
nC_8H_{17}	500
$nC_{10}H_{21}$	170
$nC_{11}H_{23}$	150
$nC_{12}H_{25}$	125
$nC_{14}H_{29}$	400
$nC_{16}H_{33}$	600

(Decyl haloalkyl sulfites:  $\mathrm{R{-}O\overset{\overset{O}{\|}}{S}O{-}C_{10}H_{21}}$)

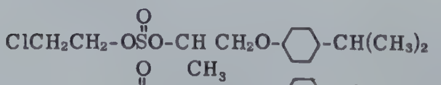
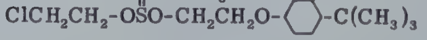
R	LD_{95} ppm
C_2H_5 -	2500
$ClCH_2CH_2$ -	170
$BrCH_2CH_2$ -	125
CCl_3CH_2 -	1000
$Cl(CH_2)_3$ -	600
 $\mathrm{ClCH_2\underset{CH_3}{\underset{\vert}{CH}}}$	500
$Cl_2C_3H_5$ -	50
C_4H_9 -	5000
$Cl(CH_2)_4$ -	400

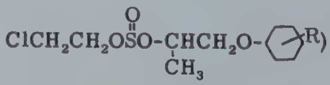
(Alkyl haloalkyl sulfites:  $\mathrm{R{-}O\overset{\overset{O}{\|}}{S}O{-}R'}$)

R	R′	LD_{95} ppm
$ClCH_2CH_2$-	nC_7H_{15}	1000
$Cl(CH_2)_3$ -	nC_7H_{15}	625
$Cl_2C_3H_5$-	nC_7H_{15}	125
$ClCH_2CH_2$-	$nC_{12}H_{25}$	125
$Cl(CH_2)_3$ -	$nC_{12}H_{25}$	125
$Cl_2C_3H_5$ -	$nC_{12}H_{25}$	75

(Substituted Aryl oxyalkyl 2- chlorethyl sulfites: )

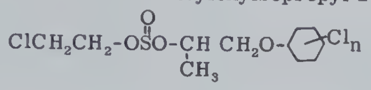
C_nH_{2n}	R	LD_{95} ppm
$-CH_2CH_2$ -	H	1250
$-CH(CH_3)CH_2$ -	H	600
$-CH_2CH_2$ -	pCl	250
$-CH(CH_3)CH_2$	pCl	60
$-CH_2CH_2$ -	$pC(CH_3)_3$	50
$-CH_2CH_2CH_2$ -	$pC(CH_3)_3$	20
$-CH(CH_3)CH_2$	$pC(CH_3)_3$ (=Aramite)	10

Compound	LD_{95} ppm
	20
	50

(Ring substitution: )

R	LD_{95} ppm
H	600
p-CH_3	100
p-$CH(CH_3)_2$	20
o-$CH(CH_3)_2$	20
p-$CH(CH_3)C_2H_5$	10
p-$C(CH_3)_3$ = Aramite	10
p-$C(CH_3)_2C_2H_5$	16
p-cyclohexyl	25

(Ring chlorine substitution of Aryloxyisopropyl 2-chloroethyl sulfites


)

Cl_n	LD_{95} ppm
H	600
p-Cl	60
2,4-diCl	20
2,4,5-triCl	50
penta-Cl	150

(1) None of the foregoing compounds is more toxic than Aramite for Tetranychus bimaculatus. None betters the low toxicity of Aramite for insects predatory on mites, for low mammalian toxicity, for high ovicidal action and lack of hazard for plants. Many sulfites are highly toxic for T. bimaculatus; others are not toxic. Most simple, symmetrical compounds are too inactive; some highly active compounds are too phytotoxic at acaricidal dosages.

d) Resistance to acaricides: 2867

(1) As an aerosol with methyl chloride, Aramite, which gave 100% kill of an ordinary strain of Tetranychus bimaculatus, showed only a 2% kill of a strain resistant to several acaricides such as Parathion, Para-Oxon, Methyl parathion, HETP, TEPP, Tetraisopropyl pyrophosphate, Sulfotepp, DMC.

e) See other data for Aramite in comparative tables under the general treatment of Miticides or Acaricides.

25

CALCIUM ARSENATE (Tri-calcium arsenate)

$CaHAsO_4$; $Ca_5H_2(AsO_4)_4$; $Ca_3(AsO_4)_2$; $[Ca_3(AsO_4)_2]_3.Ca(OH)_2$ in indefinite mixture with unreacted $Ca(OH)_2$, $CaCO_3$.

GENERAL [Refs.: 353, 2815, 1059, 757, 2226, 1542, 484, 3099]

Long used as a powerful stomach insecticide, destructive to the midgut epithelia of insects, particularly to control chewing, leaf and fruit eating insects, for example, boll weevil, bollworm, cotton leafworm, corn earworm, etc. Intensely poisonous with a high toxic hazard for man and all animal life. Dangerous to wild life, beneficial insects and honeybees. Phytotoxic potential very high, depending on variables of weather, humidity, etc. Like other arsenical insecticides, it is being largely superseded by modern, synthetic, organic agents. Consult the general statement on Arsenic, Arsenicals in the present work.

PHYSICAL, CHEMICAL

Commercial calcium arsenate, for insecticidal use, is not a single chemical entity, but an indefinite, complex mixture of several arsenates of calcium (whose formulae are given above) with an excess of calcium hydroxide. It is made by allowing arsenic acid (produced by oxidizing arsenic trioxide to arsenic pentoxide with nitric acid) to react with calcium hydroxide in such a proportion that arsenates more basic than dicalcium hydrogen arsenate result. Conditions of temperature, concentration, duration of the reaction are important, and influence the physicochemical nature of the product. The commercial product is ordinarily dyed pink, as a safety measure, and is alkaline in reaction. The active ingredient is considered to be $Ca_3(AsO_4)_2$ and the form most suitable for application to plants is held to be $Ca_3(AsO_4)_2 \cdot Ca(OH)_2$, which is unstable below 35°C. Commercial calcium arsenates are unstable in presence of CO_2 and water, breaking down to yield calcium carbonate and dicalcium hydrogen arsenate, a substance whose appreciable water solubility greatly enhances the phytotoxic hazard.

Calcium arsenate is a white, flocculent, finely divided powder with an average particle diameter as low as $1\text{-}2\ \mu$. It is higher in As_2O_5 content than acid lead arsenate, q.v., having 46-64%. It lacks the adhesive properties of lead arsenate. Melting point and density are variable. Taste: Bitter, acrid; odor: Slight, like lime; practically insoluble in water, soluble in dilute acid media; stable in alkaline solution; unstable in acid solution; slightly corrosive to metal containers and spraying equipment. Commercial calcium arsenate should contain at least 70% tricalcium arsenate (arsenate element 26%, arsenic in water soluble form 0.7%). Accumulates in the soil.

Formulations: Dusts (pure or in inert diluents); wettable powders; various mixtures with DDT, DDD, sulfur, parathion, (with all of which it is compatible), and other insecticides.

a) Often used on cotton in alternate application with BHC, a fast killer with a short residual effect, while calcium arsenate is a slow killer with a long residual effect. Used chiefly as a dust on field crops and forests.

TOXICOLOGICAL

1) Toxicity for higher animals:

a) LD_{50} for mammals: 35-100 mg/k; maximum allowable concentration as arsenic element: 0.15 ppm. 129, 2120

b) Acute toxicity:

Animal	Route	Dose	Dosage (mg/k)	
Rat	or	LD	20	3198
Rabbit	or	LD	40	3198
Rabbit	or	LD_{50}	50	1870
Dog	or	LD_{50}	38	1870

c) Chronic toxicity: Consult the general statement on Arsenic, Arsenicals, for data on chronic arsenosis and arsenic poisoning.

(1) Residues of ca. 650 ppm, or less, on alfalfa forage were fatal to cattle. 347

(2) Applied at 2 lbs per acre to alfalfa (residue: 10-90 ppm) no hazard; cattle, others, winter fed on alfalfa sprayed at 3 lbs per acre showed no symptoms; alfalfa sprayed at 6 lbs per acre depressed normal weight gain in cattle, horses, sheep. 1063

(3) On alfalfa, sprayed at 8 lbs per acre (residue: 140 ppm), a horse or cow, consuming 30 lbs forage a day. receives a daily dose of arsenic (calculated as AS_2O_3) less than the daily tolerated dose of 2000 mg. 2593

2) Phytotoxicity:

a) High phytotoxic hazard due to the formation of water-soluble arsenic compounds which may be enhanced under particular circumstances of weather, type of plant and use. 353, 2815, 129, 2120, 1059, 757

(1) Damage is done to foliage, fruit, stems, roots, depending on circumstance.

(2) Unsafe, hazardous, at all times, on stone fruits, for example, peach, cherry, plum, apricot, etc. 2557

(3) Even a normally safe spray application may severely burn apple foliage in cool, damp weather. 97

(4) Applied to coniferous forests, as dust at 40 lbs per acre, may seriously burn foliage. 3025

(5) Cotton is not ordinarily damaged at recommended levels and rates of application; iron, copper, lead, zinc oxides act as "safeners" on cotton. 286

b) Phytotoxic effects due to accumulation in, and "poisoning" of soils:

(1) Applications for control of boll weevil on cotton may seriously injure soil for subsequent crops; sandy soils are more susceptible than "heavier" soils; gray loams are more susceptible than red soils. 590, 23, 22, 21, 591

(2) Lima beans, on sandy loams which have received 500 lbs per acre, will not germinate; in clay loams, receiving the same amounts, yields were only 15% of normal. 2795

(3) As measured on the basis of yield of *Setaria italica* (millet), in pot experiments, soils may show resistances to calcium arsenate injury of the following order: 1174, 104, 264, 844

(a) Practically pure quartz sand at 4 lbs As_2O_5 per acre: Injured; yield reduced by one-half.

(b) Soils with 20% colloid content: Average resistance; at 192 lbs As_2O_5 per acre yield reduced by one-half.

(c) Soils with 60% colloid content: High resistance; at 2112 lbs As_2O_5 per acre yield reduced by one-half.

(4) Soils which have accumulated 30 ppm of arsenic from calcium arsenate application, as dusts for boll weevil control, are rendered unfit for other crops as well as cotton. Hazard is increased on coarse soils poor in humus. 48 lbs per acre are particularly harmful to the roots of cotton plants. 618

(5) Phytotoxicity of calcium arsenate to crop plants under various conditions of soil and dosage: 618

Soil Type	Place	Dosage (lbs/acre)	Effect	Crop
Heavy	Clay, South Carolina	1000	None	Cereals, Cotton
Heavy	Clay, South Carolina	1000-1500	Injury	Vetch, Cow peas
Heavy	Clay, South Carolina	"large amounts"	None	Soybean
Sandy loam	Norfolk, S. Carolina	200- 300	Serious Injury	Soybean
Silty clay	Crowley, S. Carolina	50	Injury; yield ↓ 45%	Rice
Sandy loam	Crowley, S. Carolina	150	Injury, yield ↓ 65%	Rice

(a) Lima and snap beans and turnips were killed by applications of 1000, 2000 lbs per acre in the top 3 inches of soil. All other vegetable crops were sensitive and damaged to greater or lesser degree.

(6) Phytotoxicity of calcium arsenate to leaves of the cranberry bean, dipped in suspensions of various concentrations and using the humid chamber method: 108

Concentration (%)	% Of Leaf Area Injured
.05	19
.1	56
.125	65
.2	53
.3	72

3) Toxicity for insects: (N.B. how toxicity may vary for different samples)

Insect	Route	Dose	Dosage (mg/g)	Remarks	
Alabama argillacea (5th instar)	or	LD_{50}	0.25 (.07-.46)	Ca arsenate sample 1.	1103
Alabama argillacea (5th instar)	or	LD_{50}	0.18 (.09-.21)	Ca arsenate sample 2.	1103
Alabama argillacea (5th instar)	or	LD_{50}	0.19 (.07-.22)	Ca arsenate sample 3.	1103
Alabama argillacea (5th instar)	or	LD_{50}	0.12 (.07-.15)	Ca arsenate sample 4.	1103
Alabama argillacea (5th instar)	or	LD_{50}	0.18 (.08-.20)	Ca arsenate sample 5.	1103
Alabama argillacea (5th instar)	or	LD_{50}	0.72 (.51-1.0)	Ca arsenate sample 6.	1103
Anticarsia gemmatilis	or	LD_{50}	0.11 (.08-.21)	Death in 20-48 hrs.	944
Apis mellifera (adult)	or	LD_{50}	0.7 μg/bee	Particle size fine-medium; as As.	1852
Apis mellifera (adult)	or	LD_{50}	0.6 μg/bee	Commercial product; as As element.	1852, 231
Apis mellifera (adult)	or	LD_{50}	1.3 μg/bee	Coarse particle size; as As element.	1852, 231
Apis mellifera (adult)	or	LD_{100}	0.9 μg/bee	Fine particle size; as As element.	231
Apis mellifera (adult)	or	LD_{100}	1.0 μg/bee	Medium particle size; as As element.	231
Apis mellifera (adult)	or	LD_{100}	2.0 μg/bee	Coarse particle size; as As element.	231
Apis mellifera (adult)	or	—	0.1 μg/bee	1% kill after 3 days; as As element.	231
Apis mellifera (adult)	or	—	0.8 μg/bee	88% kill after 3 days; as As element.	231
Apis mellifera (adult)	or	—	1.6 μg/bee	100% kill after 3 days; as As element.	231
Ascia rapae (larva)	or	LD_{50}	>1.39	Ca arsenate sample 1.	1381
Ascia rapae (larva)	or	LD_{50}	0.74 (.60-1.04)	Death in 20-48 hrs.	944
Autographa brassicae (larva)	or	LD_{50}	0.50 (.33-.66)	Death in 20-48 hrs.	944
Bombyx mori (larva)	or	LD_{50}	>0.78	Ca arsenate sample 1.	1381
Bombyx mori (larva)	or	LD_{50}	0.26 (.123-332) =	Intermediate zone. Sample 2.	1381
Heliothis armigera (5th instar)	or	LD_{50}	0.21 ±.083	±= 5% confidence limits.	108
Hyphantria cunea (larva)	or	LD_{50}	2.0 (.42-4.77)	Death in 20-48 hrs.	944
Leptinotarsa decemlineata (4th instar)	or	LD_{50}	0.052 ±.008	±= 5% confidence limits.	108
Melanoplus differentialis ♂ (av. wgt=.88g)	or	LD_{50}	0.18 ±.12	±= 5% confidence limits.	108
Melanoplus differentialis ♀ (av.wgt=p.45g)	or	LD_{50}	0.16 ±.086	±= 5% confidence limits.	108

Calcium arsenate + Paris green

Insect	Route	Dose	Dosage (mg/g)	Remarks	
Alabama argillacea (5th instar)	or	LD_{50}	0.04 (.03-.08)	Ca arsenate 90: Paris green 10.	1103
Alabama argillacea (5th instar)	or	LD_{50}	0.09 (.05-.15)	Ca arsenate 92.5: Paris green 7.5.	108

Rhagoletis pomonella: Mean time for 50% kill; deposit from 1g/100 cc suspension = 76 hrs. 2259
Rhagoletis fausta: Mean time for 50% kill; deposit from 1g/100 cc suspension = 62 hrs. 2259

Diabrotica duodecempunctata (Adult): Time to 50% kill after 1 min roll in 1g of 25% dust = 210 minutes. 108
Diabrotica duodecempunctata (Adult): Time to 50% kill after 1 min roll in 1g of 50% dust = 145 minutes. 108
Diabrotica duodecempunctata (Adult): Time to 50% kill after 1 min roll in 1g of 75% dust = 90 minutes. 108
Diabrotica duodecempunctata (Adult): Time to 50% kill after 1 min roll in 1g of 100% dust = 80 minutes. 108

a) Also consult section treating of Bees and Insecticides, in this work.
b) Toxicity of calcium arsenate to Hippodamia convergens, a beneficial predatory lady-bird beetle: 1450
  (1) Depending upon method used for application of calcium arsenate at 1 1/2 lbs per 50 gallon water spray, the average kill ranged, for adults and older larvae, from 24 (16-31)% to 100%. Eggs and 1st instar larvae showed none or slight mortality from application by any one of 4 different methods.

4) Mode of action, pharmacological, physiological, pathological considerations: Insects:
a) Consult the general section treating of Arsenic and Arsenicals in this work.
b) The marked influence of pH upon the solubility of calcium arsenate exerts great influence upon its action and toxicity for various insects e.g.: 3108
  (1) Solubility of calcium arsenate declines to virtually 0 in alkaline media, thus Bombyx mori may excrete considerable quantities unchanged because the pH of the digestive tract is between pH 8-9.
  (2) Dixippus, on the other hand (gut pH 6.6) is actively and quickly poisoned by calcium arsenate.
  (3) Acid lead arsenate, for the reasons stated above, although containing 1/3 less arsenic than calcium arsenate, is just as effective as calcium arsenate against Carpocapsa pomonella (larvae) with a gut (stomach) pH of 8.5. 2113
c) Histological examination of Heliothis armigera larvae, after oral poisoning with calcium arsenate, revealed disorganization and disintegration of the cells of the midgut epithelium. 502
  (1) Large patches of epithelium were sloughed into the lumen.
  (2) Basement membrane and muscle intact, although chromatinic clumping was apparent in muscle cell nuclei.
  (3) Peritrophic membrane apparently undamaged.

5) Calcium arsenate in the economic control of insects:
   - a) Vs. Alabama argillacea: The insecticide of choice; DDT does not control. 2226
     3 xs as toxic as DDT for A. argillacea at 5 days interval application using 4-8 lbs/acre.
   - b) Vs. Pieris (=Ascia) rapae: 25% dusts gave 78% control. Residue hazard. 2226
   - c) Vs. Protoparce sexta, P. quinquemaculata: 50% dusts gave control. 2226
   - d) Lymantria dispar: Controlled by dusts at 40 lbs/acre. 837
   - e) Vs. Cirphis unipuncta: 20 lbs/acre gave 90% control. 2428, 2796
   - f) Vs. Heliothis armigera: Less efficient than copper arsenate which is 2 times as effective. 1264, 323
   - g) Vs. Choristoneura fumiferana: Only poor control at 30 lbs/acre. 353
   - h) Vs. Carpocapsa pomonella: At a disadvantage vis-a-vis lead arsenate because of phytotoxicity to apple trees. 726
   - i) Effective vs. Loxostege similalis, but replaced by DDT. 3287
   - j) Vs. Plutella maculipennis: Gives control, but is inferior to nicotine sulfate and supplanted 160, 445, 1480,
     by DDT. 2705, 3234
   - k) Vs. Clysia ambiguella: Supplanted by DDT. 3287
   - l) Vs. Melittia satyriniformis: Supplanted by DDT. 375
   - m) Vs. Nematus ribesii: Supplanted by rotenone. 375
   - n) Vs. Leptinotarsa decemlineata: 0.6% suspension controls, but supplanted by DDT. 3287
   - o) Vs. Epitrix cucumeris, E. tuberis, E. fuscula: Gives only ca 35% control. Replaced by DDT. Vs. 375, 1052, 1525,
     E. tuberis: Increases the effectiveness of DDT, 0.1% DDT + 0.5% calcium arsenate recommended.1255, 349, 1202
   - p) Vs. Cylas formicarius: Far surpasses Paris green in control of. 561
   - q) Vs. Pantormus leucoloma: Effective, but surpassed by DDT. 3388
   - r) Anthonomus grandis controlled by undiluted dusts at 7-10 lbs/acre; toxaphene, DDT, lindane are 285, 2438,
     superior. Aldrin, Dieldrin probably surpass all. 1657

26

CALCIUM CYANIDE (Cyanogas®)

$Ca(CN)_2$ Molecular weight: 92.12

GENERAL

[Refs.: 484, 353, 2815, 1059, 757, 129, 2120, 1925, 605, 611, 3261, 2250, 2561, 3153, 3154, 3152]

Used as a source of HCN in circumstances in which a fumigant action with hydrocyanic acid gas is desired. Calcium cyanide reacts slowly with water in moist air yielding HCN. Widely used as a space and storage fumigant and in limited soil fumigation in the field and greenhouse. Used in the fumigation of stored cereals and in the control of scale insects on glasshouse plants. May be mixed with grain in steel storage bins or elevators at the rate of 10 lbs per 1000 bushels of grain. Like all cyanides intensely poisonous and hazardous to all living animals adequately exposed.

PHYSICAL, CHEMICAL

A gray, crystalline, solid or powder; soluble in water; unstable in the presence of moisture, especially in the 2250
presence of such a weak acid as H_2CO_3, breaking down with the evolution of HCN. Highly poisonous and must be 2561
kept dry in appropriate, tightly sealed containers. The amount of HCN evolved in a normally moist atmosphere 129
amounts to ca. 25% by weight of the calcium cyanide used. The decomposition by water proceeds at humidities as low as 25% relative atmospheric humidity. The commercial product should not contain less than 42% calcium cyanide. Formulated as dusts, flakes, granules. Formulations with ca 55% cyanogen content may be made by combining HCN, calcium carbide, 2% water. 1 1/4 ounces of 30% cyanogen $Ca(CN)_2$ = to 20 cc liquid HCN.

TOXICOLOGICAL

1) The toxicity of calcium cyanide is due to the cyanide ion and the hydrogen cyanide evolved by the substance. (See the treatment of Hydrogen cyanide in this work.)
   - a) Precautions must be taken in situations where the use of calcium cyanide in enclosed spaces may lead to high concentrations of hydrocyanic acid vapor.
     - (1) This vapor is toxic not only by inhalation but by skin absorption.
     - (2) Appropriate masks should be used where high concentrations are possible. Avoid inhalation, skin contact.
   - b) Symptoms of exposure to small doses: Dizziness, headache, shortness of breath, which, on continued exposure, may result in convulsions, coma and collapse.
   - c) Residue levels drop quickly on airing.
   - d) Use of calcium cyanide as a rodenticide indicates the hazard involved for domestic and wild animals.

2) Uses of calcium cyanide in the control of insects:

a) For the toxicity and biological properties of "cyanide", and hydrogen cyanide consult the section on Hydrogen cyanide in this work.

b) For night fumigation of greenhouses; other fumigations:

(1) Calcium cyanide (dust, flakes, granules) scattered on floors at rate of 1/4 - 1/3 ounce per 1000 ft^3 at 55°-75°F. 757

(2) Plants should be unwatered and exposed for 1 hour.

(3) Fumigation of carnation plants in glasshouses at rate of 0.75 oz per 1000 ft^3, = to 0.13 mg/l HCN, for exposure periods of 3 hrs; may result in damage to plants, particularly if soil is damp and plants unshaded. 281

(4) To control Phenococcus gossypii on greenhouse chrysanthemums:

(a) Overnight exposures, 3-6 fumigations at weekly interval, using 3/16 - 5/8 ounce per 1000 ft^3, resulted in high mortality, with 5-15% of eggs also being killed.

(b) Pseudococcus citri, P. maritimus, are distinctly < susceptible to Ca(CN)$_2$ fumigation than Phenococcus gossypii. 2620

(5) Used in control of Tarsonemus latus (adults, larvae, eggs) and Heliothrips haemorrhoidalis on greenhouse plants, almost 100% (98.5%) mortalities may be achieved using 1 oz. (28.4g) per 1000 ft^3. 2869

(a) Higher mortalities of Tarsonemus latus are had at 56°-55°F than at 66°-80°F.

(6) Fumigations of orchard trees may be carried out under appropriate tents with exposures, at night, of 1 hr at 50°-75°F using Ca(CN)$_2$ dust. 757

(7) 5-7 g 28% cyanogen Ca(CN)$_2$ per 1000 ft^3 is recommended for greenhouse fumigation, although resistant insects may need 2 oz per 1000 ft^3. 3260

(8) For the control of Diaspis boisduvalli, (Boisduval's scale) on Cattleya in low concentration; overnight greenhouse fumigation: 280

Number Weekly Fumigations	Ounces 40% Ca(CN)$_2$/1000 ft^3			% Mortality (Mature ♀♀)
	1st Week	2nd Week	3rd Week	
0 (control)				7.3
1	1/15	—	—	37.3
1	1/10	—	—	81.7
1	1/8	—	—	84.4
2	1/10	1/10	—	97.6
2	1/10	1/8	—	96.9
3	1/10	1/8	1/10	98.4

(a) Slight injury to older leaves may be expected.

(9) May be used in fumigation of ant nests outdoors. 757

c) Other uses:

(1) As a paint in linseed oil, has been used to control Saperda candida (white-headed apple borer). 2481

(2) Effective against Blissus leucopterus (chinch bug).

d) Effectiveness of calcium cyanide in the control of certain insects under greenhouse conditions: 2264

(1) Vs. Trialeurodes vaporariorum:

Number Of Fumigations	Dosage Ounces/1000 ft^3	Temperature (°F)	Relative Humidity (%)	% Kill
2	1/12	62-71	—	60
2	1/8	60-67	90	70-80
4	1/6	54-70	72-95	80
1	1/5	64	79	80
11	1/4	58-67	71-87	90-100
17	1/3	56-68	84-87	50-100
11	1/2	52-70	—	50-100
2	2/3	58-70	—	100
4	3/4	59-77	—	100

(2) Vs. other insects:

Insect	Plant	Dosage Oz/1000 ft^3	Temp. (°F)	Relative Humidity (%)	% Kill	No. Fumigations
Myzus persicae	—	1/7	71	73	80	1
Myzus persicae	—	1/5	62	79	70	2
Myzus persicae	—	1/4	58-62	83-89	90	3
Myzus persicae	—	1/3	52-66	83-94	98	8
Myzus persicae	—	3/7	60	89	90	1
Myzus persicae	—	1/2	52	—	100	1
Macrosiphum gei	—	1/7	60	86	75	2
Macrosiphum gei	—	1/6	65	—	60	1
Macrosiphum lineatum	—	3/8	55	88	50	2
Myzus circumflexus	—	1/4	53-65	83-89	78	5
Myzus circumflexus	—	1/3	59	68	80	1
Myzus circumflexus	—	1/2	53-55	88-90	90	2
Macrosiphoniella sanborni	—	1/4	53	—	100	1
Macrosiphoniella sanborni	—	1/3	53-55	—	100	2

(2) Vs. other insects:

Insect	Plant	Dosage Oz/1000 ft^3	Temp. (°F)	Relative Humidity (%)	% Kill	No. Fumigations
Aphis rumicis		1/5	59	89	90	1
Thrips tabaci	Carnation	1/3	60	—	10	—
Thrips tabaci	Carnation	1/2	62	—	partial control	—
Thrips tabaci	Carnation	2/3	59	—	65	—
Heliothrips haemorrhoidalis	Tomato	1/4	59-60	72-73	30-40	—
Heliothrips haemorrhoidalis	Arums	3/7	60	89	70	—
Heliothrips bicinctus	Smilax	1/4	59	97	10-20	—
Parthenothrips dracenae	Kentia palm	1 1/2	60	—	90	—

27

CARBAMATES AND CARBAMIC ACID ESTERS AS INSECTICIDES; GENERAL TREATMENT

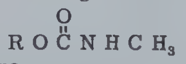
(See the several individual carbamic acid esters in this work.)

GENERAL REMARKS

[Refs.: 1120, 2942, 1132, 1133, 1317, 1316, 3272, 2552]

a) The general class of substances known as carbamic acid esters contains numerous compounds intensely toxic for higher animals.
b) Recently, this group has been found to contain substances which have a powerful action as insect toxicants.
   (1) Examples of these new insecticides are compounds named: Dimetan, Pyrolan, Isolan, q.v.
c) For mammals and other vertebrates, physostigmine, m-dimethyl-aminophenyl N-methyl carbamate methiodide or prostigmine, are all well known cholinergic drugs, powerful in action and belonging to the class of carbamic acid esters.
d) As insecticides, these substances are characterized by a swift, pyrethrin-like effect, when tested on Musca domestica.
   (1) Toxic on contact to aphids, thrips, bed bugs, granary weevils, etc.
   (2) Low effectiveness vs. spider mites.
   (3) Residual action is of short duration.
   (4) Some have shown an effective systemic action, being absorbed by plants via leaves and/or roots, in quantities toxic to thrips and aphids feeding on the treated plants.
e) Insect poisoning by these substances is sharply distinguishable from the toxic action of the well-known chlorinated hydrocarbons.
   (1) The action is more rapid, resembling that of phosphoric acid esters.
   (2) They include potent inhibitors, in vivo and in vitro, of choline esterase(s).

1) Toxicity for insects of substances of the general formula

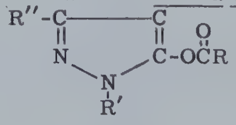


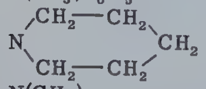
$$ROC(=O)NHCH_3$$

is closely dependent upon structure.

a) Toxicity of pyrazolyl carbamates for Musca domestica: 1317, 1316

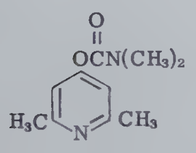
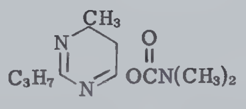
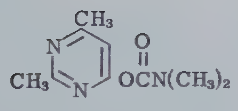
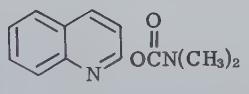
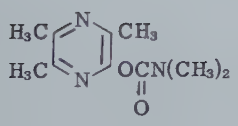
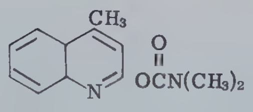
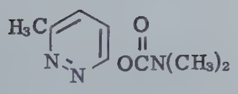
(1) General formula:



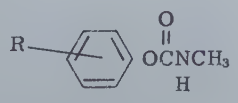
R	R′	R″	Effective Concentration (mg/cm^2)
$N(CH_3)_2$	C_6H_5	CH_3	0.01
$N(C_2H_5)_2$	C_6H_5	CH_3	10
$N(C_3H_7)_2$	C_6H_5	CH_3	1
$N(CH_3)C_6H_5$	C_6H_5	CH_3	1
	C_6H_5	CH_3	0.1
$N(CH_3)_2$	p-$CH_3C_6H_4$	CH_3	10
$N(CH_3)_2$	p-$CH_3OC_6H_4$	CH_3	nil
$N(CH_3)_2$	m-ClC_6H_4	CH_3	10
$N(CH_3)_2$	2,3-diClC_6H_3	CH_3	nil
$N(CH_3)_2$	3,5-diClC_6H_3	CH_3	nil

R	R′	R″	Effective Concentration (mg/cm²)
$N(CH_3)_2$	p-NCC_6H_4	CH_3	nil
$N(CH_3)_2$	p-$O_2NC_6H_4$	CH_3	0.1
$N(CH_3)_2$	C_6H_5	CH_3	0.1
$N(CH_3)_2$	C_6H_5	CH_3	1
$N(CH_3)_2$	C_6H_5	CH_3	10
$N(CH_3)_2$	H	CH_3	0.01
$N(CH_3)_2$	CH_3	CH_3	0.01
$N(CH_3)_2$	C_2H_5	CH_3	0.01
$N(CH_3)_2$	n-C_3H_7	CH_3	0.01-0.1
$N(CH_3)_2$	iso-C_3H_7	CH_3	0.01
$N(CH_3)_2$	$CH_2CH{=}CH_2$	CH_3	0.01
$N(CH_3)_2$	n-C_4H_9	CH_3	0.01
$N(CH_3)_2$	$CH_2CH(CH_3)_2$	CH_3	0.01
$N(CH_3)_2$	$CH(C_2H_5)CH_3$	CH_3	0.01-0.1
$N(CH_3)_2$	$C(CH_3)_3$	CH_3	0.001
$N(CH_3)_2$	$CH_2C(CH_3){=}CH_2$	CH_3	0.01
$N(CH_3)_2$	C_5H_{11}	CH_3	0.1
$N(CH_3)_2$	$CH_2CH_2CH(CH_3)_2$	CH_3	0.001
$N(CH_3)_2$	C_8H_{17}	CH_3	1-10
$N(CH_3)_2$	CH_2CH_2F	CH_3	0.01-0.1
$N(CH_3)_2$	$CH_2CH_2OC_2H_5$	CH_3	0.001

b) Toxicity of heterocyclic carbamates vs. Musca domestica: 1317, 1316

Compound	Effective Conc. (mg/cm²)	Compound	Effective Conc. (mg/cm²)
	0.001		0.1
	0.1		Inactive
	0.1		Inactive
	Inactive		

c) Contact toxicity, anticholinesterase activity and hydrolysis of phenyl-N-methylcarbamates: 1848



R	Cholinesterase Inhibition$_{50}$ (I_{50}) (moles)	Musca domestica LD_{50} Topical (μg/g)	Heliothrips haemorrhoidalis LC_{50} (%)	K hydrolysis at 32.5°C
H	2×10^{-4}	70	0.015	2.5×10^{2}
o-CH_3	1×10^{-4}	500	.008	2.6×10^{2}
m-CH_3	8×10^{-6}	50	.003	3×10^{2}
p-CH_3	1×10^{-4}	500	> .1	—
m-C_2H_5	1×10^{-5}	250	.02	—
o-isoC_3H_7	6×10^{-6}	100	.00018	54.5
p-iso C_3H_7	7×10^{-5}	> 500	.023	—
o-tert C_4H_9	6×10^{-6}	75	.00015	28
m-tertC_4H_9	4×10^{-7}	50	.00008	4
p-tert C_4H_9	1.5×10^{-4}	> 500	> .1	—
o-NO_2	5×10^{-3}	250	—	3.4×10^{6}
m-NO_2	2×10^{-4}	> 500	.02	—
p-NO_2	3×10^{-3}	> 500	> .01	3.4×10^{5}
o-Cl	5×10^{-6}	75	> .01	2.0×10^{3}
m-Cl	5×10^{-5}	100	.007	1.7×10^{3}
p-Cl	2.4×10^{-4}	> 500	.018	1.0×10^{3}
o-C_6H_{11}	1.4×10^{-6}	> 500	.0007	—
5-di-CH_3	6×10^{-6}	60	.0015	—
m-$(CH_3)_2N$	8×10^{-6}	500	.0005	20
m-$(CH_3)_2N \cdot CH_3I$	1.6×10^{-8}	> 500	.02	—
2-CH_3-5-isoC_3H_7	2×10^{-6}	> 500	.00025	—
5-CH_3-2-isoC_3H_7	1.4×10^{-6}	30	.0003	—
2,3,5-tri-ch_3	6×10^{-6}	500	.00023	—
2,4-di-tertC_4H_9	1×10^{-3}	> 500	> .1	—
2,4-di-Cl	5×10^{-4}	> 500	.009	—
2,4-di-NO_2	1×10^{-3}	> 500	.03	—
2CH_3-4,6-di-NO_2	4×10^{-3}	> 500	> .01	—
2,6-di-CH_3O-3,5-di-NO_2	7×10^{-5}	> 500	.004	—
2,4,5-tri-Cl	1.4×10^{-5}	> 500	.02	—
2,4,6-tri-Cl	1.7×10^{-5}	> 500	.04	—

d) Toxicity and anticholinesterase activity of carbamic acid esters vs. various insects:

(1) vs. Musca domestica: 1119, 1848

Compound	LD_{50} (μg/g)	I_{50} (Moles)
Prostigmine bromide	> 500	4×10^{-8}
N,N-Dimethyl carbamic acid ester of (2-hydroxy-5-phenyl benzyl) dimethyl ammonium chloride	> 500	3×10^{-8}
N,N-Dimethyl carbamic acid ester of (3-hydroxy-2-pyridyl methyl)-di methylamine HCl	> 500	8×10^{-8}
Dimetan	3.2 (Oral)	—
Pyrolan	3.2 (Oral)	—

(2) Vs. other insects: 2659

Compound	Deltocephalus dorsalis		D. cucurbitae		Ceratitis capitata	
	LD_{50}, or (μg/g)	I_{50} (moles)	LD_{50}, or (μg/g)	I_{50} (moles)	LD_{50}, or (μg/g)	I_{50} (moles)
Dimetan	117	5×10^{-7}	128	6.5×10^{-7}	92	5.6×10^{-7}
Isolan	—	7.2×10^{-8}	—	8×10^{-8}	—	1.2×10^{-7}
Pyrolan	1.3	2×10^{-8}	1.2	7.8×10^{-8}	4.6	2.8×10^{-8}

3) Pharmacology, mode of action etc.:

a) Physostigmine affects transmission in insect nerve. Symptoms develop swiftly: 505, 2682, 3096

(1) Trembling, ataxia, falling, yield to prostration with recurrent tremor followed by death or sometimes recovery.

(2) Applied to ventral nerve cord (Periplaneta americana) at the 6th abdominal ganglion at 5×10^{-5} M, gave after-discharge following a presynaptic volley of nerve impulses; at 10^{-4} M gave synaptic block; transmission along giant fiber axon: No effect before 10^{-3} M concentration.

(a) Effect may be removed by washing.

(3) Effect in insects (as in mammals) is consistent with a postulate of cholinesterase inhibition.

b) It has been postulated by some that the charge on the carbamate molecule influences physiological action, for instance: 3322

(1) Prostigmine does not penetrate crab or squid axon; does not affect conduction.

(2) Physostigmine penetrates and affects conduction.

(3) m-Dimethylamino phenyl dimethyl carbamate, although but 1/100th as active as prostigmine as a cholinesterase inhibitor (tertiary amine analogue of prostigmine), penetrates the nerve axon to block conduction.

c) *In vitro* choline esterase inhibition by prostigmine was not affected by pH. 2342
   (1) Molecule remained positively charged over the pH range.
   (2) Physostigmine is cationic at pH 6 becoming neutral at pH 10.
      (a) Gives maximum ChE inhibition at pH 6.
   (3) LD_{50} of physostigmine, by injection in *Locusta migratoria*, = 20-25 μg/g; LD_{50} of prostigmine (same route) = 1200 mg/g. 1583

d) *Utimate mode of action in insects appears to depend on inhibition of insect ChE.* 2231
   (1) Toxic carbamates with acetylcholine-like configurations are all effective ChE inhibitors.
   (2) Correlation of contact toxicity for *Musca domestica* of N-methylcarbamates of substituted phenols with ChE inhibitory activity is good.
   (3) *Musca*, paralyzed by 5 μg/insect doses of n-tert-butyl phenyl N-methylcarbamate (the most toxic compound), showed 71% inhibition of brain ChE; the related m-dimethylaminophenyl N-methyl carbamate gave 52% inhibition.
   (4) Inhibition was not as complete as that given by organophosphorus insecticides.
      (a) Evidence of the reversible nature of the inhibition, with partial dissociation from the enzyme, seems to be supported by ability of *Musca* to recover after several hours. 505
   (5) *In vivo* and *in vitro* ChE inhibitory action may differ markedly for a given carbamate, suggesting *in vivo* metabolic alterations, or interactions, to yield highly active, or less active, products. 2659
   (6) Pyrolan and dimetan exhibit a certain specificity toward the various esterases. 2552

28

CARBON DISULFIDE (Carbon bisulfide, Carbon disulphide or bisulphide)

CS_2 Molecular weight: 76.14

GENERAL

[Refs: 2662, 129, 2120, 2815, 353, 757, 1059, 2706, 314, 539, 1925, 605, 1327, 2260, 611, 3261, 1024, 2414, 2375, 197, 55, 3187, 2840, 541, 1533, 1534]

(Also see general treatment of Fumigants in this work.)
An insecticidal fumigant whose properties, in control of some insects, have been known and used since their discovery in France in 1854. First used to control grape *Phylloxera* on the roots of vines. Following discovery of its usefulness (and it was probably the first of the synthetic insecticides of organic nature), carbon disulfide advanced rapidly in general use, although it is now being replaced by other fumigants, or mixtures of other fumigants and carbon disulfide, to reduce the serious hazards involved in its use. Preparation is by heating sulfur and coke in the electric furnace.

The vapor of carbon disulfide is highly toxic, and the effects of continued exposure to appreciable amounts may be cumulative and attended by pathological changes which may be fatal.

Carbon disulfide has found extensive use in household, warehouse, ship, soil, and stored products fumigation. In the fumigation of grain, it is to be remembered that germination potential is seriously impaired. Being exceedingly toxic to all living things, carbon disulfide cannot be used as a greenhouse fumigant. With proper precautions, it has been used to fumigate dormant nursery stock and as a soil fumigant in vineyards and elsewhere. As an emulsion, it has been applied to the soil to control such soil-dwelling insects as Japanese beetle and wireworms. In this last connection distinct nematocidal properties may be noted.

PHYSICAL, CHEMICAL

Colorless to yellow, highly inflammable, liquid; impurities customarily present confer a noxious, highly unpleasant, smell; m.p. - 111.6°C; b.p. 46.3°C; $d_4^{20°}$ (as liquid) 1.263 as gas 2.63 (air = 1); bulk density: 359 cc = 1 pound, 10.5 pounds = 1 gallon; $n_D^{15°}$ 1.6315; v.p. 361 mm Hg at 25°C, 297.5 mm Hg at 20°C; vapor saturation at 25°C 1470 mg/l; 77 lbs/1000 ft^3 = the maximum amount which can be present as a vapor at 68°F; flash point (ca) 20°C; at 1 volume to 99 volumes air = an explosive mixture; ignites spontaneously at 125°-135°C; explosive in air at a lower limit of 1.2%; soluble in water to 0.22g/100 cc at 32°C (or 1 cc:530 cc water); miscible with most organic solvents, notably anhydrous alcohol, chloroform, ether; a lipoid solvent. Highly poisonous and to be used only with appropriate precautions to guard against personal and public hazard. Fire hazard is reduced by using carbon disulfide in appropriate proportions with carbon tetrachloride. Voids fire insurance. *Formulations*: Usually used alone; emulsions with alkali (thiocarbonates), soap, alcohol and solutions have been on the market; mixtures, notably with carbon tetrachloride, to reduce fire hazard. In general use at 5-30 lbs per 1000 ft^3.

Other physical, chemical and miscellaneous data:

a) Maximum weights of CS_2 which can, under various conditions, exist in vapor form in a 1000 ft^3 fumigating chamber: 2671

(1) N.B. CS_2 is liquid at 32°F.

Temperature (°F)	Vapor Pressure	Lbs/1000 ft^3
32	127 mm Hg	36
59	246 mm Hg	65
68	297 mm Hg	77
77	357 mm Hg	91
86	433 mm Hg	109
95	519 mm Hg	128
104	617 mm Hg	150
113	729 mm Hg	175
122	760 mm Hg	179

b) 1 mg/l of CS_2 (molecular weight 76) = 322 ppm; 1 ppm = 0.0031 mg/l. 2815

c) Sorption and penetration of CS_2 in patent flour compared with certain other common fumigants: 3013

(1) Sorption by patent flour, in 5 hr surface exposures, 25°C, exposed to 200 mg fumigant/1 at standard pressure:

Fumigant	B.P.(°C)	Mg Fumigant Sorbed (After 5 hrs Exposure)	Sorption Ratio	
Carbon disulfide	46	10.9	1	(Arbitrary Standard)
Methyl acetate	57.5	68.5	6.3	
Carbon tetrachloride	76.7	14.7	1.3	
Ethylene dichloride	84	41.0	3.8	
Trichloroethylene	87.1	25.6	2.3	
Propylene dichloride	96	34.1	3.1	
Chloropicrin	112	78.3	7.2	
Tetrachloroethylene	120	113.7	10.4	

(2) Penetration through flour after 24 hrs exposures under standard conditions:

Fumigant	Mg Fumigant Passed Through In 24 hrs.	Penetration Ratio
Carbon disulfide	154.6	1
Methyl acetate	108.2	.70
Carbon tetrachloride	119.7	.78
Ethylene dichloride	111.3	.72
Trichloroethylene	95.8	.62
Propylene dichloride	94.8	.61
Chloropicrin	65.1	.42
Tetrachloroethylene	57.6	.37

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage	Remarks	
Rabbit	sc	LD	300 mg/k		1982
Rabbit	inh	LC	16 mg/l	6 1/4 hrs exposure; death in 7 days.	1962
Cat	inh	LC	23 mg/l	Continuous exposure, 3 hrs.	1960
Cat	inh	LC	7400 ppm	Continuous exposure, 3 hrs.	1960
Cat	inh	LC	122 mg/l	48 minute exposure; death in 12 hrs.	1960
Sunfish	Medium	LC	100-127 ppm	In tap H_2O; death in 1 hr.	2811
Trout	Medium	LC	5000 ppm	7 min exposure; death 2 days later.	939

a) Poisoning is ordinarily by inhalation of the highly toxic vapor. 197, 1221

b) Chronic intoxication, by vapor inhalation, is the chief hazard for man. 197

(1) 2000 ppm (1:500 in air) brought on giddiness, vomiting, severe headache, in 30 minutes.

(2) Repeated daily exposure (1:15,000 concentration) yielded ill health, malaise, cachexia.

(3) Maximum concentration tolerated without serious effect for 1 hr: ca 4800 ppm 2221, 3187

(4) Maximum tolerated concentration: 60 minutes at 1.5 mg/l; 8 hrs. at 1 mg/l. 1665

c) Daily exposures should not exceed concentrations of 20 ppm. 55

d) Space concentration limits: Massachusetts, 15 ppm; New Jersey, 20 ppm; Wisconsin, California, 1 ppm. 129

e) Probable safe concentration for indefinite exposure: 0.01 mg/l or 3.2 ppm. 1665

f) Contact with skin and eyes should be carefully avoided. 129

2) Pharmacological, pharmacodynamic, physiological etc., higher animals:

a) Carbon disulfide is a liposoluble central nervous system poison. 1221, 1220

b) Symptoms (acute) involve CNS depression. 1221, 1220

(1) Exposure (30 min or >) to >1000 ppm yielded initial excitement followed by CNS depression; followed by coma succeeded by terminal convulsions; ended by death in respiratory failure.

c) Chronic exposure to sub-acute concentrations: 1221, 1220
   - (1) Chronic symptoms due to extensive CNS damage.
   - (2) Multiple peripheral neuritis leading to paralysis was commonly noted.
   - (3) Optic nerve particularly susceptible; visual disturbances due to optic nerve atrophy.
   - (4) Corneal anaesthesia; corneal hyporeflexia is characteristic.
   - (5) Rotary nystagmus (of vestibular origin) is frequently seen.
   - (6) Prolonged, sub-acute exposure may cause emotional instability, sexual impotency, dementia, mania, paranoia followed by other psychoses. 318
   - (7) Parkinsonian symptoms suggest involvement of basal ganglia in the toxic process.
   - (8) Sleep and appetite disturbed; gastrointestinal symptoms, weakness, anemia, weight loss, general debility may attend chronic exposure.

d) Treatment is mainly symptomatic; recovery is prolonged; damage may be irreversible. 1221

3) Phytotoxicity:

a) Too phytotoxic for any but specialized applications. Not applicable to glasshouse or growing plants. 353, 129
Toxic to some seeds, particularly impairing germination in those of high moisture content, but less damaging to dry seeds. Kills many perennial weeds. 757

b) May be used, without damage, to fumigate fresh fruit, but thorough airing is necessary. 757, 1501

c) Under proper conditions may be locally injected into trees and shrubs to control burrowing insects such as *Zeuzera pyrinae*, *Prionoxystus robiniae*, *P. macmurtrei*, *Podosesia syringae*, *Tremex columbae*.

d) Soil fumigation at base of *Vitis* controls root *Phylloxera vitifoliae* without undue damage to the vine. 2226

4) Toxicity for insects:

(N.B.: To obtain values in terms of lbs/1000 ft³ divide mg by 16.4)

a) LC_{50} and LC_{95} values for several stored products insects (adult stage), exposed in empty 100 ft³ fumatoria at 70°F: 2005

Insect	LC_{50} (mg/l) 2 hrs Exposure	LC_{50} (mg/l) 6 hrs Exposure	LC_{95} (mg/l) 2 hrs Exposure	LC_{95} (mg/l) 6 hrs Exposure
Sitophilus granarius	103	43	149	65
Sitophilus oryzae	48	36	80	50
Zabrotes pectoralis	84	46	106	64
Stegobium paniceum	110	42	168	62
Tribolium confusum	> 179	75	> 179	103
Acanthoscelides obtectus	54	29	90	43
Oryzaephilus surinamensis	119	40	> 179	68
Rhizopertha dominica	72	31	108	49

b) Other toxicity data:

Insect	Route	Dose	Dosage (mg/l)	Remarks	
Attagenus piceus (larva)	fumig	LC_{50}	88	Exposure 5 hrs, 25°C; empty flask fumigation.	2817
Bruchus obtectus (adult)	fumig	LC_{50}	22	Exposure 5 hrs, 25°C; empty flask fumigation.	2816
Dacus dorsalis (naked eggs 23-26 hr old)	fumig	LC_{50}	53	Exposure 2 hrs, 71°-80°F; empty vessel fumigation.	255
Dacus dorsalis "	fumig	LC_{95}	92	Exposure 2 hrs, 71°-80°F; empty vessel fumigation.	255
Dacus dorsalis (larva)	fumig	LC_{50}	56	Exposure 2 hrs, 71°-80°F, empty vessel fumigation.	255
Dacus dorsalis (larva)	fumig	LC_{95}	89	Exposure 2 hrs, 71°-80°F; empty vessel fumigation.	255
Ephestia küehniella (eggs)	fumig	LC_{100}	502	Exposure 1 hr; vacuum held at 0 inches.	608
Ephestia küehniella (eggs)	fumig	LC_{100}	502	Exposure 1 hr; vacuum held at 29 inches.	608
Limonius californicus	fumig	LC_{50}	31.5		1957
Limonius californicus	fumig	LC_{100} (ca)	51		1957
Limonius californicus	fumig	LC_{50}	4.2	Exposure 5 hrs. 77°F, in liter flasks with 500g soil.	1958
Limonius canus	fumig	LC_{50}	4.2	Exposure 5 hrs, 77°F, in liter flasks with 500 g soil.	1958
Oryzaephilus surinamensis (adult)	fumig	LC_{50}	34	Exposure 5 hrs, 25°C, empty flask.	2816
Rhizopertha dominica (adult)	fumig	LC_{50}	20	Exposure 5 hrs, 25°C empty flask.	2817
Sitophilus granarius (adult)	fumig	LC_{50}	40	Exposure 5 hrs, 25°C empty flask.	2816
Sitophilus granarius (adult)	fumig	LC_{99}	66	Exposure 5 hrs. 25°C empty flask.	2816
Sitophilus granarius (adult)	fumig	LC_{50}	23.8	Exposure 24 hrs, 80°F, at surface of wheat.	2009
Sitophilus granarius (adult)	fumig	LC_{95}	32.5	Exposure 24 hrs, 80°F, at surface of wheat.	2009
Sitophilus granarius (adult)	fumig	LC_{50}	27.6	Exposure 24 hrs, 80°F, 2 in below surface of wheat.	2009
Sitophilus granarius (adult)	fumig	LC_{95}	40.1	Exposure 24 hrs, 80°F, 2 in below surface of wheat.	2009
Sitophilus granarius (adult)	fumig	LC_{50}	29.7	Exposure 24 hrs, 80°F, 5.5 in below surface of wheat.	2009

b) Other toxicity data:

Insect	Route	Dose	Dosage (mg/l)	Remarks	
Sitophilus granarius (adult)	fumig	LC_{95}	43.0	Exposure 24 hrs, 80°F, 5.5 in below surface of wheat.	2009
Sitophilus oryzae (adult)	fumig	LC_{50}	26	Exposure 5 hrs, 25°C, empty flask.	2816
Sitophilus oryzae (adult)	fumig	LC_{99}	40	Exposure 5 hrs, 25°C, empty flask.	2816
Tenebriodes mauritanicus (adult)	fumig	LC_{50}	.102cc/ 5lb corn	Exposure 24 hrs, 30°C, in 5 lb lots shelled corn.	2603
T. mauritanicus (adult)	fumig	LC_{50}	.129 g/ 5lb corn	Exposure 24 hrs. 30°C, in 5 lb lots shelled corn.	2603
T. Mauritanicus (adult)	fumig	LC_{95}	.111 cc/ 5 lb corn	Exposure 24 hrs. 30°C, in 5 lb lots shelled corn.	2603
T. mauritanicus (adult)	fumig	LC_{95}	.104 g/ 5 lb corn	Exposure 24 hrs. 30°C, in 5 lb lots shelled corn.	2603
Tribolium castaneum (adult)	fumig	LC_{50}	28	Exposure 5 hrs, 25°C, empty flask.	2816
Tribolium confusum (adult)	fumig	LC_{50}	61	Exposure 5 hrs, 25°C, flask fumigation.	2816
T. confusum (adult)	fumig	LC_{99}	91	Exposure 5 hrs, 25°C, flask fumigation.	2816
T. confusum (adult)	fumig	LC_{50}	64	No absorbent present, 25°C, 760 mm Hg.	1013
T. confusum (adult)	fumig	LC_{50}	147	In presence of flour, 25°C, 760 mm Hg.	1013
T. confusum (adult)	fumig	LC_{50}	55	Exposure 5 hrs, empty containers.	1798
T. confusum (adult)	fumig	LC_{50}	63	Exposure 5 hrs, 25°C, low Rel. Humidity no > 10%.	2008
T. confusum (adult)	fumig	LC_{50}	63	Exposure 5 hrs, 25°C, high Rel. Humidity 50%-70%.	2008
T. confusum (egg)	fumig	LC_{50}	147	Exposure 5 hrs, 25°C, low Rel. Humidity no > 10%.	2008
T. confusum (egg)	fumig	LC_{50}	87	Exposure 5 hrs, 25°C, high Rel. Humidity 50%-70%.	2008
T. confusum (adult)	fumig	LC_{50}	29.8	Exposure 24 hrs, 80°F, surface of whole wheat.	2009
T. confusum (adult)	fumig	LC_{95}	43.0	Exposure 24 hrs, 80°F, surface of whole wheat.	2009
T. confusum (adult)	fumig	LC_{50}	30.5	Exposure 24 hrs, 80°F, 2 in below surface of wheat.	2009
T. confusum (adult)	fumig	LC_{95}	43.9	Exposure 24 hrs, 80°F, 2 in below surface of wheat.	2009
T. confusum (adult)	fumig	LC_{50}	34.5	Exposure 24 hrs, 80°F, 5.5 in below surface of wheat.	2009
T. confusum (adult)	fumig	LC_{95}	54.0	Exposure 24 hrs, 80°F, 5.5 in below surface of wheat.	2009
T. confusum (egg 1 da old)	fumig	LC_{50}	220.6	Exposed at 25°C, R.H. 60% Note response at different ages of various life cycle stages.	3013
T. confusum (egg 3 da old)	fumig	LC_{50}	169.1	Exposed at 25°C, R.H. 60%	3013
T. confusum (egg 5 da old)	fumig	LC_{50}	146.8	Exposed at 25°C, R.H. 60%	3013
T. confusum (egg 7 da old)	fumig	LC_{50}	95.5	Exposed at 25°C, R.H. 60%	3013
T. confusum (larva 1 da old)	fumig	LC_{50}	66.2	Exposed at 25°C, R.H. 60%	3013
T. confusum (larva 7 da old)	fumig	LC_{50}	24.5	Exposed at 25°C, R.H. 60%	3013
T. confusum (larva 14 da old)	fumig	LC_{50}	27.0	Exposed at 25°C, R.H. 60%	3013
T. confusum (larva 21 da old)	fumig	LC_{50}	39.6	Exposed at 25°C, R.H. 60%	3013
T. confusum (larva 28 da old)	fumig	LC_{50}	47.3	Exposed at 25°C, R.H. 60%	3013
T. confusum (larva 35 da old)	fumig	LC_{50}	50.4	Exposed at 25°C, R.H. 60%	3013
T. confusum (pupa 1 da old)	fumig	LC_{50}	127.7	Exposed at 25°C, R.H. 60%	3013
T. confusum (pupa 3 day old)	fumig	LC_{50}	119.4	Exposed at 25°C, R.H. 60%	3013
T. confusum (pupa 5 da old)	fumig	LC_{50}	178.0	Exposed at 25°C, R.H. 60%	3013
T. confusum (pupa 7 da old)	fumig	LC_{50}	174.0	Exposed at 25°C, R.H. 60%	3013
T. confusum (pupa 9 da old)	fumig	LC_{50}	119.4	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 1 da old)	fumig	LC_{50}	128.3	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 4 da old)	fumig	LC_{50}	97.6	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 7 da old)	fumig	LC_{50}	108.7	Exposed at 25°c, R.H. 60%	3013
T. confusum (adult 14 da old)	fumig	LC_{50}	90.3	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 21 da old)	fumig	LC_{50}	81.4	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 28 da old)	fumig	LC_{50}	77.7	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 35 da old)	fumig	LC_{50}	78.7	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 8 wk old)	fumig	LC_{50}	74.0	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 12 wk old)	fumig	LC_{50}	70.2	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 16 wk old)	fumig	LC_{50}	68.4	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 20 wk old)	fumig	LC_{50}	65.0	Exposed at 25°C, R.H. 60%	3013
T. confusum (adult 24 wk old)	fumig	LC_{50}	69.3	Exposed at 25°C, R.H. 60%	3013
Zabrotes subfasciatus (adult ♀♀)	fumig	LC_{50}	20	Exposure 5 hrs, 25°C, empty flask fumigation.	2817

c) Relative susceptibility to CS_2; life cycle stages, in order from most to least susceptible stage:

(1) *Ephestia*: Adult > larva > pupa. 412

(2) *Tribolium*: Larva > adult > pupa > egg. 2003

d) Toxicity of CS_2 and influence of temperature:

(1) *Tribolium confusum* (adult), exposed 5 hrs in empty fumigation flasks: 2816

Temperature (°C)	LC_{50} (mg/l)	LC_{99} (mg/l)
35°	32	40
30°	44	68
25°	61	91
20°	76	108
15°	86	140
10°	154	280
5°	140	270

(a) Time, for kill of T. confusum, must be increased 2–3 times if exposure temperature is decreased from 35°C to 25°C.

(2) Minimum time to obtain 100% kill, Tribolium confusum (adult) at various temperatures: 2996

(a) Dosage: 15 lbs/1000 ft^3.

Temperature (°C)	Time for 100% Mortality
35°	30 Minutes
30°	45 Minutes
25°	1.5 Hours
20°	2 Hours
15°	3 Hours
10°	3.5 Hours

5) Pharmacological, physiological and other considérations; insects:

a) For insects, as for higher forms, considered to be neurotoxic as a liposoluble narcotic. Most extensive uptake of the toxicant is by the insect ventral nerve cord. 353

b) Small amounts of CS_2 appear to stimulate tracheal ventilation. 3013

(1) Initial exposure of Sitophilus to sub-lethal concentrations increased the susceptibility to toxic effect of CS_2 fumigation begun a few minutes later.

c) Mortality of Tribolium and Sitophilus, exposed to CS_2 is enhanced if the post-treatment holding temperature is $>$ 25°C. 3013

d) Tribolium confusum, T. castaneum, Sitophilus oryzae are $>$ susceptible to CS_2 if small amounts of CO_2 are added. 617

6) Miscellaneous data, considerations:

a) Toxicity of CS_2 used in mixtures of various proportions with other fumigants in whole shelled corn: 2605

(1) Exposure: 24 hrs, at 30°C, in 5 lb lots of corn.

Fumigant Mixture	% by Volume	Insect	Position in Corn	LC_{50} (cc/5lbs)	LC_{95} (cc/5lbs)
CS_2 + CCl_4	80-20	Tribolium castaneum	Bottom	.064	.084
CS_2 + CCl_4	80-20	Tribolium castaneum	Top	.062	.085
CS_2 + CCl_4	50-50	T. castaneum	Top	.080	.129
CS_2 + CCl_4	50-50	T. castaneum	Bottom	.076	.110
CS_2 + CCl_4	20-80	T. castaneum	Top	.129	.202
CS_2 + CCl_4	20-80	T. castaneum	Bottom	.124	.182
CS_2,1,1-dichloro-1-nitroethane, CCl_4	20-0-80	Oryzaephilus surinamensis	Top	.171	.227
CS_2,1,1-dichloro-1-nitroethane, CCl_4	20-0-80	O. surinamensis	Bottom	.162	.206
CS_2,1,1-dichloro-1-nitroethane, CCl_4	15-5-80	O. surinamensis	Top	.106	.133
CS_2,1,1-dichloro-1-nitroethane, CCl_4	15-5-80	O. surinamensis	Bottom	.104	.127
CS_2,1,1-dichloro-1-nitroethane, CCl_4	10-10-80	O. surinamensis	Top	.063	.091
CS_2,1,1-dichloro-1-nitroethane, CCl_4	10-10-80	O. surinamensis	Bottom	.062	.078
CS_2,1,1-dichloro-1-nitroethane, CCl_4	5-15-80	O. surinamensis	Top	.038	.059
CS_2,1,1-dichloro-1-nitroethane, CCl_4	5-15-80	O. surinamensis	Bottom	.043	.061
CS_2,1,1-dichloro-1-nitroethane, CCl_4	0-20-80	O. surinamensis	Top	.030	.042
CS_2,1,1-dichloro-1-nitroethane, CCl_4	O-20-80	O. surinamensis	Bottom	.033	.049
CS_2,1,1-dichloro-1-nitroethane, CCl_4	5-5-90	Tribolium castaneum	Top	.159	.226
CS_2,1,1-dichloro-1-nitroethane, CCl_4	5-5-90	T. castaneum	Bottom	.141	.206

b) Used as a fumigant vs. Aonidiella (= Chrysomphalus) aurantii, CS_2 proved only moderately toxic being outranked by numerous other fumigants. 669

c) Dosages for practical use in fumigation of steel bins to control stored products insects, for example Sitophilus granarius, Rhizopertha dominica, Plodia interpunctella, Sitotrage cerealella, etc. 609

Dosage/1000 bushels in	Wheat	Corn	
CS_2 (alone)	1	1.5	gallon(s)
CS_2 + CCl_4 1:4	2	5	

d) Uses:

(1) Against stored products insects, most economical as a 20% mixture in CCl_4, which is effective at rate of 20 lbs/1000 ft^3. 353

(2) Horse bots, Gastrophilus spp: Oral administration (2 cc/100 lbs body wgt) kills larvae [illegible] intestinal tract of host. 2980

(3) Useful in outdoor fumigation of ant nests. 2226

(4) Once used to control Melolontha vulgaris, as well as Popilla japonica and the grubs of Lepidoderma in sugar cane. 353 1295

(5) Used at 10, 8, 6 lbs/1000 ft^3, with exposures respectively of 8, 15, 24 hrs, CS_2 gave 100% kill of all stages of Lasioderma serricorne in tobacco products. 661

(a) 4 hrs exposure did not yield, even assisted by low pressures, complete kill.

(b) The vapor readily and rapidly left cigars; no change in flavor, aroma.

(6) For various data of screening tests see Ref. 1801.

29

CARBON TETRACHLORIDE (Tetrachloromethane; Perchloromethane; Benzinoform)

CCl_4 Molecular weight: 153.84

GENERAL (Also see the general treatment of Fumigants in this work)
[Refs.: 353, 2815, 757, 1059, 539, 605, 436, 611, 342, 129, 2120, 1689, 2909, 2306]

A fumigant of comparatively low insecticidal activity, but having certain distinct advantages: Non-inflammable, non-explosive, and absorbed in low quantity by the fumigated product. Low insecticidal potential renders the cost too high for many purposes. Where long exposures are possible, carbon tetrachloride is used in grain fumigations. Use is ordinarily limited to small scale fumigations where cost is not a prime object, or where a fire hazard exists. It finds extensive use as a local, spot fumigant and in admixture with other fumigant insecticides, for instance, carbon disulfide or ethylene dichloride, to reduce fire hazard. Also, it is used to dilute more toxic substances, for example, methyl bromide or ethylene dibromide, to assist in distribution of these more toxic vapors; large amounts are used in this manner in grain fumigation. An example of dosages of carbon tetrachloride alone, and in mixture, in treatment of grain in wooden bins to protect from various stored grain insects follows:

Fumigant	Gallons / 1000 Bushels		
	Small grains (Sorghum Excepted)	Sorghums	Corn
Carbon tetrachloride	5	8	6
$CCl_4 + CS_2$ 4 : 1	3	8	6
CCl_4 + ethylene dichloride 1 : 3	6	10	6
CCl_4 + ethylene dibromide 19 : 1	3	8	6

In combination with acrylonitrile, q.v., in equal parts, carbon tetrachloride has been effective against insects of stored tobacco in closed storage as a substitute for hydrogen cyanide. It has also found use, in the past, as a nursery stock fumigant.

In vapor or liquid form, carbon tetrachloride is toxic for man, and higher animals, both by inhalation, and skin absorption. A constant exposure to more than 100 ppm in air is considered dangerous. In the presence of an open flame it is converted to phosgene and the hazard of poisoning thereby enhanced. 3199

PHYSICAL, CHEMICAL

Colorless, heavy liquid at room temperatures, not inflammable or explosive; sweetish, chloroform-like odor, m.p. -23°C; b.p. 76.7°C; $d_{4°}^{25°}$ (liquid) 1.589, $d_{4°}^{20°}$ 1.595; vapor density 5.3 (air = 1); $n_D^{20°}$ 1.4607; v.p. 114.5 mm Hg at 25°C, 159.6 mm Hg at 20°C; vapor saturation in air at 25°C 940 mg/l; practically insoluble in water (1cc: 2000 cc, 0.08g/100g at 25°C); miscible with most organic solvents, notably: Alcohols, benzene, chloroform, ether, carbon disulfide, petroleum ether, oils; carbon tetrachloride is a notable lipo-solvent which finds extensive use in dry-cleaning and elsewhere; lowest concentration detectable by odor = 72 ppm; mg/l = 158.8 ppm, 1 ppm =.0063 mg/l. 3199 2221

a) Maximum weight of carbon tetrachloride which, at various temperatures, can exist in vapor form in a 1000 ft³ fumigating chamber. CCl_4 is liquid at 32°C: 2621

Temperature °F	Vapor Pressure	Lbs/1000 ft³ in Vapor Form
32	33	19
59	71	38
68	91	48
77	115	59
86	143	73
95	176	88
104	216	100
113	263	127
122	313	149

b) Sorption by and penetration through patent flour of carbon tetrachloride: 3013
   (1) Sorption after 5 hrs exposure at 25°C of flour at standard pressure to 200 mg/l of CCl_4, surface exposure.
   (2) Penetration after 24 hrs exposure, standard temperature, pressure.
   (3) CCl_4 compared with certain other fumigants.

Fumigant	B.P.(°C)	Mg Sorbed 5 hrs.	Sorption Ratio	Mg Passed Through, 24 hrs.	Penetration Ratio
Carbon disulfide	46	10.9	1	154.6	1
Methyl Acetate	57.5	68.5	6.3	108.2	.7

Fumigant	B.P. (°C)	Mg Sorbed 5 hrs.	Sorption Ratio	Mg Passed Through, 24 hrs.	Penetration Ratio
**Carbon tetrachloride	76.7	14.7	1.3	119.7	.78
Ethylene dichloride	84	41.0	3.8	111.3	.72
Trichloroethylene	87.1	25.6	2.3	95.8	.62
Propylene dichloride	96	34.1	3.1	94.8	.61
Chloropicrin	112	78.3	7.2	65.1	.42
Tetrachloroethylene	120	113.7	10.4	57.6	.37

Formulations: Alone, or in combination, at various proportions, with carbon disulfide, ethylene dichloride, ethyl acetate, acrylonitrile etc.

TOXICOLOGICAL 3199

1) Acute toxicity for higher animals:
   a) Maximum allowable concentration for man: 25 ppm; maximum therapeutic dose: 1.5 cc—3 cc (as vermifuge). 2221
   b) Threshold limit: 50 ppm. 55
   c) Maximum tolerated concentration (based on Guinea Pigs) tolerable without serious symptoms: For 1 hr: 60 mg/l; for 8 hrs: 10 mg/l. 1665
   d) Probable safe concentration for indefinite exposure: 0.69 mg/l (100 ppm.) 1665

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	12,800	Pure substance.	885
Mouse	sc	LD	32,000	Death in 24 hrs.	1070
Rat	or	LD_{50}	7,460 (5730-9770)		2907
Rat	ct	LD_{50}	6,670 (5070-8780)		2907
Rabbit	or	LD	6380-9975		1902
Cat	sc	LD_{33}	4785		466
Dog	or	LD	4000	Death in 24 hrs.	195
Dog	or	LD	25,000		1902
Dog	iv	MLD	125	In oil; death in 30 mins.	195

			(mg/l)	(ppm)		
Mouse	inh	LC_{50}	59.95 ± .86	9528	Exposure 7 hrs; death in 8 hrs.	3024
Mouse	inh	MLC	65-70	10,320-13,160	Exposure 2 hrs.	1938
Rat	inh	LC_{50}	150.5	23,900	Exposure 1/2 hr; death in 14 days.	2940
Cat	inh	LC	90	14,300	Exposure 70 min; death in 1-17 days.	2594

2) Chronic, sub-acute toxicity, higher animals: 3199
   a) In subacute toxicity, due to repeated exposure to carbon tetrachloride, the liver is the primary site of injury. The kidneys also may suffer. 1221
      (1) Liver cirrhosis may be produced in experimental animals by repeated exposure. 2953
      (2) Severe, macrocytic anemia, partly due to liver damage, partly to direct action on bone marrow, may arise. 2953
      (3) In susceptible strains of mice, experimental hepatoma has been induced with carbon tetrachloride. 924
      (4) Diet and dietary supplements play a role in susceptibility and resistance to the heptotoxic or nephrotoxic action of carbon tetrachloride. 1221
      (5) Skin irritation, dermatitis, mucous membrane irritation, bronchitis, conjunctivitis may follow exposure to the vapor, which may be absorbed by the unbroken skin. Hypertension and visual field constriction are also known. 1221
      (6) Constant exposure to 100 ppm is dangerous; exposures of 1 hour to 10,000 ppm (or less) may arouse symptoms of short duration. Toxic potential enhanced in drunkeness and alcoholism. 2221 1953
      (7) Exposure to 100 ppm is permitted by New Jersey; maximum allowable concentration, Massachusetts = 40 ppm. Precautions against inhalation and skin contamination are necessary.
   b) Rats and monkeys have lived indefinitely at 100 ppm concentrations; laboratory animals, continuously exposed to 400 ppm, have shown liver and kidney damage. The jaundice, evident at 200 ppm and indicating liver injury, is reversed by regeneration when exposure ceases. 2909

3) Pharmacological, pharmacodynamic, physiological, etc.: 3199
   a) Orally taken, carbon tetrachloride is a gastrointestinal irritant which yields warm, burning sensations. 1221
   On the skin it is irritant, rubifacient. Irritant action stimulates intestinal peristalsis. 1220
   b) On the central nervous system, action is analogous to that of chloroform: 1221, 1220
      (1) Irregularly descending depression, first of the higher centers, then the cord, lastly the medulla.
      (2) By inhalation, absorption is swift, and central nervous action predominant.
      (3) In oral administration, the concentration in the blood is not enough for marked central effect and symptoms are usually giddiness, drowsiness.
   c) In circulatory effects, carbon tetrachloride resembles chloroform, being toxic to the heart, and depressant to heart muscle. Central vasomotor depression, if high enough concentrations reach the blood stream, may lower the blood pressure. 1221 1220
   d) Absorption of inhaled vapor from the respiratory tract occurs readily. 1221
      (1) 1 part in 1000 parts air is the upper limit man may breath safely.
      (2) Gastrointestinal absorption is less ready and is affected by numerous variables.

(3) A single oral dose is less toxic than the same quantity in divided doses.
(4) Solvents, for instance alcohol, by enhancing absorption, enhance oral toxicity.

e) In the body, appreciable amounts are metabolized appearing in exhaled air (in radio-isotope studies) as CO_2, in urine as urea, bicarbonate. 1221

f) Symptoms of acute poisoning: 1221, 1220
(1) Early symptoms of inhalation poisoning referrable to CNS are: Fullness in head, diziness, headache, stupor, unconsciousness. Progressive depression, medullary paralysis follow on continued exposure. Myocardial, vasomotor effects followed by cardiovascular collapse.
(2) Oral poisoning adds other signs of gastrointestinal origin: Pain, vomiting, nausea, diarrhea.
(3) Apparent recovery from immediate effects does not preclude late toxic signs of acute poisoning—hepatotoxic, nephrotoxic signs, the latter seeming to predominate in inhalation poisoning, the former in ingestion poisoning.
(4) Hepatic lesions resemble those produced by chloroform, namely, a diffuse, central necrosis. Renal lesion may be placed in the category of lower nephron nephrosis.

g) Therapeutic use is made of carbon tetrachloride as an anthelminthic agent, particularly against hookworm, in carefully controlled dosage and administration because of its toxicity. 1221 1220

4) Phytotoxicity:

a) Does not affect the germination quality of wheat. Not used on the growing plant by direct contact, by which method it proves dangerously toxic. 129

5) Toxicity for insects:
n.b. mg/l ÷ 16 = lbs/1000 ft³.

Insect	Route	Dose	Dosage (mg/l)	Remarks	
Cimex lectularius (adult)	Fumig	ca$LC_{95}LC_{100}$	> 50		2622
Cimex lectularius (adult)	Fumig	LC_{50}	113		416
Cimex lectularius (older nymphs)	Fumig	caLC_{95}-LC_{100}	> 50		2622
Cimex lectularius (eggs)	Fumig	caLC_{95}-LC_{100}	> 50		2622
Dacus dorsalis (naked eggs 23-26 hr old)	Fumig	LC_{50}	>167.8	Exposure 2 hrs, 71°-80°F, empty vessel.	255
Dacus dorsalis (larva, 3rd instar)	Fumig	LC_{50}	>167.8	Exposure 2 hrs, 71°-80°F, empty vessel.	255
Ephestia kuehniella	Fumig	LC_{50}	448		416
Sitophilus granarius (adult)	Fumig	LC_{50}	360	Exposure 5 hrs, 25°C, flask fumigation.	2816
Sitophilus granarius (adult)	Fumig	LC_{50}	592		416
Sitophilus granarius (adult)	Fumig	LC_{99}	859	Exposure 5 hrs, 25°C, flask fumigation.	2816
Sitophilus oryzae (adult)	Fumig	LC_{50}	160	Exposure 5 hrs, 25°C, flask fumigation.	2816
Sitophilus oryzae (adult)	Fumig	LC_{50}	473		416
Sitophilus oryzae (adult)	Fumig	LC_{50}	64(.04±.002cc/l)	Exp. 24 hrs, 30°C, empty space.	2605
Sitophilus oryzae (adult)	Fumig	LC_{95}	83(.052cc/l)	Exp. 24 hrs. 30°C, empty space.	2605
Sitophilus oryzae (adult)	Fumig	$LC_{99.99}$	104(.065cc/l)	Exp. 24 hrs, 30°C, empty space.	2605
Sitophilus oryzae (adult)	Fumig	LC_{99}	559	Exposure 5 hrs, 25°C, empty flask.	2816
Tenebrioides mauritanicus	Fumig	LC_{50}	.276cc/5 lb, .438g/5 lb	Exp. 24 hrs, 30°C, in 5 lb lots of shelled corn.	2603
Tenebrioides mauritanicus	Fumig	LC_{95}	.455cc/5 lb,.723g/5 lb	Exp. 24 hrs, 30°C, in 5 lb lots of shelled corn.	2603
Tineola bisselliella	Fumig	LC_{50}	352		416
Tribolium castaneum (adult)	Fumig	LC_{50}	137		416
Tribolium castaneum (adult)	Fumig	LC_{50}	105.5	Exposure 2 hrs, 30°C.	1689
Tribolium castaneum (adult)	Fumig	LC_{99}	209.1	Exposure 2 hrs, 30°C.	1689
Tribolium confusum (adult)	Fumig	LC_{50}	185	Exposure 5 hrs, 25°C, flask fumigation.	2816
Tribolium confusum (adult)	Fumig	LC_{50}	66	Exposure 5 hrs, empty container.	1060
Tribolium confusum (adult)	Fumig	LC_{99}	405		2816
(Fumigation with CCl_4, Acrylonitrile, 50:50)					
Dacus dorsalis (naked eggs, 23-26 hr old)	Fumig	LC_{50}	3.7	Exposure 2 hrs, 71-80°F, empty vessel.	255
Dacus dorsalis (naked eggs, 23-26 hr old)	Fumig	LC_{95}	11	Exposure 2 hrs, 71-80°F, empty vessel.	255
Dacus dorsalis (larva 3rd instar)	Fumig	LC_{50}	1.7	Exposure 2 hrs, 71-80°F, empty vessel.	255
Dacus dorsalis (larva 3rd instar)	Fumig	LC_{95}	4.9	Exposure 2 hrs, 71-80°F, empty vessel.	255

a) Temperature and toxicity of CCl_4 to Tribolium confusum (adult): 2816
(1) Exposure 5 hrs, 25°C, empty flask fumigation:

Temperature (°C)	LC_{50} (mg/l)	LC_{99} (mg/l)
35	75	225
30	125	490
25	185	405
20	225	564
15	230	589
10	250	535
5	Incomplete Kill, <50%	

b) Fumigation of *Tribolium confusum* and *Sitophilus granarius*, exposed at the surface and at various depths in whole wheat grain: Exposure 24 hrs, 80°F, in 28 l cans, 14.5 in high, 12.5 in diameter, containing 30 lbs whole wheat at a depth of 8 inches with 6.25 in free space above: 2009

Fumigant	Depth in grain (in)	T. confusum		S. granarius	
		LC_{50} (mg/l)	LC_{95}	LC_{50} (mg/l)	LC_{95}
Carbon tetrachloride	Surface	55.0	110	93	230
Carbon tetrachloride	2	55.0	110	90	210
Carbon tetrachloride	5.5	55.0	90	90	200
CCl_4 + acrylonitrile 1:1	Surface	11	18	5	9.8
CCl_4 + acrylonitrile 1:1	2	12.5	21	10	19
CCl_4 + acrylonitrile 1:1	5.5	20.2	36	12	19
CCl_4 + ethylene chlorobromide 95:5	Surface	27.9	52	30	80
CCl_4 + ethylene chlorobromide 95:5	2	28.2	51.8	40	85
" " "	5.5	32	68.1	52	94
" " 90:10	Surface	18.1	38.3	26	50
" " "	2	20	52.1	30	64
" " "	5.5	33.9	77	43	80
CCl_4 + ethylene dibromide 95:5	Surface	28.7	42	25.8	47.2
	2	31	58	37	69
	5.5	42.7	70	44.2	> 113.9
CCl_4 + ethylene dichloride 1:3	Surface	21.1	47	63	> 190
	2	28.1	56.7	72.8	> 190
	5.5	29.8	59.5	81.5	> 190

(1) Dosages of CCl_4, and CCl_4 in combination with other fumigants, required for 95% mortality at the least effective level in wheat (5.5 inches) exposed 24 hrs, 80°F, conditions as in "b" above. *Tribolium confusum* (adult), test insect: 2009

Fumigant	Mg/l For LC_{95}	cc/1/2 Bushel Wheat for LC_{95}	Remarks
CCl_4	110	1.90	Least effective at surface of wheat.
CCl_4, acrylonitrile 1:1	36	.84	
CCl_4 25%, ethylene chloride 75%	59.5	1.25	
CCl_4 95%, ethylene chlorobromide 5%	68.1	1.3	
CCl_4 95%, ethylene dibromide 5%	70.0	1.2	
CCl_4 90%, ethylene chlorobromide 10%	77	1.35	

c) Toxicity of CCl_4 alone, and with other fumigants, for various insects exposed in 5 lb lots of shelled corn at various depths in the container; temperature 30°C: 2605

Fumigant	Insect	Exposure (hrs)	Position	LC_{50} ← cc/5lbs corn	→ LC_{95}
CCl_4	*Sitophilus oryzae*	24	Top	0.171	0.229
"	" "	24	Bottom	.160	.236
"	*Tribolium castaneum*	24	Top	.136	.174
"	" "	24	Bottom	.129	.164
"	" "	72	Top	.204	.298
"	" "	72	Bottom	.178	.280
"	" "	168	Top	.165	.199
"	" "	168	Bottom	.157	.193
"	*Oryzaephilus surinamensis*	24	Top	.150	.214
"	" "	24	Bottom	.136	.191
CCl_4, ethylene dichloride (standard mixture)	*T. castaneum*	24	Top	.247	.370
	"	24	Bottom	.250	.316
CCl_4 + CS_2 20%:80% v/v	*T. castaneum*	24	Top	.062	.085
" "	"	24	Bottom	.064	.084
50%:50%		24	Top	.080	.129
" "	"	24	Bottom	.076	.110
" 80%:20%	"	24	Top	.129	.202
" "	"	24	Bottom	.124	.182
CCl_4, 1,1-dichloro-1-nitroethane, β-methylallyl chloride 90%;5%;5% v/v	"	24	Top	.124	.174
" "	"	24	Bottom	.119	.147

d) Fumigation of certain fumigant resistant insects (*Tineola bisselliella*, *Attagenus piceus*, *Anthrenus vorax*) with CCl_4 in combination with several other fumigants. Conditions: 500 ft³ fumigation vault, 24 hrs exposure, insects buried in vials in "overstuffed furniture". Amount (lowest) yielding 100% kill in 24 hrs. exposure: 2670

Substance	Parts By Volume	Substance	Parts By Volume	Temp. (°F)	Lbs/1000f^3 for 100% Kill
(alone)	1	Ethylene dichloride	3	85	6
CCl_4				85	30
"	1	Ethylene dichloride	3	65	12
"	7	tert-Butyl chloride	3	83	12
"	3	Ethyl iodide	1	85	5
"	7	tert-Butyl alcohol	3	85	20
"	7	n-Propyl formate	3	85	11
"	3	Isopropyl formate	1	85	14
"	3	sec-Butyl formate	2	85	8
"	3	Isobutyl formate	2	85	9
"	3	Isoamyl formate	2	85	7
"	3	Isopropyl acetate	3	83	15
"	1	Diethyl carbonate	1	83	> 30

e) Dosages of CCl_4 and CCl_4 in combination with other fumigants for use in fumigation of steel bins against such stored products insects as Sitophilus oryzae, S. granarius, Rhizopertha dominica, Plodia interpunctella, Sitotrage cerealella, etc.: 609

Material	Gals/1000 Bu Wheat	Gals/1000 Bu Corn
CCl_4	3	4
CCl_4 + CS_2 4:1	2	5
Chloropicrin 2 lb + CCl_4 to make 1 gal	1.5	1
CCl_4 + ethylene dichloride 1:3	4	5
1,1-Dichloro-1-nitroethane 2 lb + CCl_4 to make 1 gal	1.5	1
β-Methylallyl chloride 1 lb + " " " " "	2	2
CCl_4 + ethylene dichloride 1:3 + 10% methyl bromide	2	2
CCl_4 + methyl bromide 9:1	2	2
CCl_4 + propylene chloride 1:3 + 10% methyl bromide	2	2

(1) Carbon tetrachloride should not be used at temperatures < 24°C, 75°F. 1689

(2) In combination with methyl bromide, methyl formate, ethylene dichloride CCl_4 tends to reduce the toxicity of these various fumigants to values below the level observed when they are used alone. 1689

(3) Not nearly as effective a fumigant as CS_2, larger quantities being required at much greater cost. However, CCl_4 overcomes the fire hazard which attends use of CS_2. 2816

(4) Used in box car fumigation vs. rice weevil, flour weevil, granary weevil, Indian meal moth at 45 lbs per 1000 ft^3; at 85°F, complete kill of these insects may be had with 6 lbs per 1000 ft^3. 129

(5) The concentration of CCl_4 required to give 100% mortality of a "population" of Sitophilus granarius, 52.4 lbs per 1000 ft^3, is near the limit which can exist in form of CCl_4 vapor (59.1 lb at 25°C) in a 1000 ft^3 fumigation chamber. 2671

(6) Unsatisfactory as a fumigant vs. Lasioderma serricorne in stored cigars. 661

f) Minimum time for obtaining 100% mortality of Tribolium confusum, exposed to CCl_4 at 20 lbs/1000 ft^3 at various temperatures. 2996

°C	Minimum Time for 100% Kill (Hrs)
35	1.5
30	3.25
25	7
20	ca 12

g) Comparison of LC_{50}, LC_{99}, values (Tribolium castaneum) of CCl_4, and other extensively used fumigants. Exposures 2 hrs, at 30°C, flask fumigation: 786

Fumigant	LC_{50}	LC_{99}
CCl_4	105.5	209.1
Methyl bromide	14.0	17.5
Methyl formate	28.0	43.4
Ethylene dichloride	95.5	149.5

6) Pharmacological, pharmacodynamic, physiological considerations: Insects:

a) Acts, in insects, as a narcotic, lipophilic, liposoluble, neurotoxic toxicant. 353

(1) Narcosis is achieved after an initial phase of excitation, which is followed by paralysis and finally death.

b) Ephestia kuehniella larvae, exposed to CCl_4, reveal a sudden increase of heart pulsation as a prelude to a steady, progressive, deceleration of the heart. 353

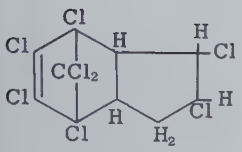
c) CCl_4, in the insect body, penetrates and concentrates almost exclusively in the ventral nerve cord. 2601

d) Mortality of insects, exposed to CCl_4, is enhanced if the insects are held, post-fumigation, at temperatures > 25°C, but within physiological range. 3013

For screening data, trials against various insects, consult Ref. 1801.

30

CHLORDAN(E) (1, 2, 4, 5, 6, 7, 8, 8-Octachloro-2, 3, 3a, 4, 7, 7a-hexahydro-4,7-methanoindene; 1, 2, 4, 5, 6, 7, 8, 8-Octachloro-4, 7-methane-3a, 4, 7, 7a-tetrahydroindane; Velsicol 1068; CD-68; Octa-klor. Octachlorodihydrodicyclopentadiene.)



$C_{10}H_6Cl_8$

Molecular weight: 409.828

GENERAL Refs.: [353, 2231, 1953, 2815, 1756, 1757, 1988, 2640, 2639, 1395, 379, 89, 3150, 1067, 1950, 3199]

An insecticide of the cyclodiene group which also contains heptachlor, aldrin, dieldrin, isodrin, endrin, toxaphene q.v., characterized as cyclic hydrocarbons, highly chlorinated and with an endomethylene bridged structure. Produced (save toxaphene) by the Diels-Alder diene reaction. Chlordane, and its closely related compounds mentioned above, has found an extensive application as an agricultural and household insecticide, particularly in control of locusts, grasshoppers, crickets, soil insects, insects predatory on cotton, cockroaches, flies, etc. Toxic by mouth, skin inhalation; precautions necessary. Persistent stomach, contact poison for most insects with marked residual toxicity.

PHYSICAL, CHEMICAL [Refs.: 2231, 1953, 129, 2090, 2089, 3014, 3195, 353, 89, 2394, 642, 3150, 3199]

1) Formed by reaction of hexachlorocyclopentadiene with cyclopentadiene ⟶ hexachlorodicyclopentadiene (chlordene) which is then chlorinated to contain 68%-69% chlorine, as indicated by the empirical formula given above. The technical product is a viscous, amber liquid of aromatic cedar-like odor; the refined substance is a yellowish liquid; b.p. (tech.) 175°C at 2 mm Hg; d_{25} 1.59-1.63; $n_D^{25°}$ 1.56-1.57; v.p. (refined) 1×10^{-5} mm Hg at 25°C; insoluble in water; miscible with aliphatic and aromatic hydrocarbons, esters, ketones, ethers, and most organic solvents, including petroleum oils; for example deodorized kerosene; viscosity, 69 poises at 25°C, decreased by heating to 120-140°F, at which temperature chlordane may be sprayed directly; dechlorinated by alkalis to yield non-toxic products by loss of hydrogen chloride, the reaction being catalysed by iron in traces; incompatible with any alkaline solvent, diluent, carrier, emulsifier.

2) The technical product is a mixture of various isomers, of varying physiological activity, but chromatographically separable. Among these constituents the following are described:
   a) α-Chlordane, cis-2, 3, 4, 5, 6, 7, 8, 8-octachloro-2, 3, 3a, 4, 7, 7a-hexahydro-4, 7-methanoindene, m.p. 102-104°C, inert in 0.04 Methanol-NaOH;
   b) β-Chlordane, trans-2, 3, 4, 5, 6, 7, 8, 8-octachloro-2, 3, 3a, 4, 7, 7a-hexahydro-4, 7-methanoindene, m.p. 104-106°C, ready dechlorination in 0.04 Methanol-NaOH;
   c) 1, (or 3a,) 4, 5, 6, 7, 8, 8-Heptachloro-3a, 4, 7, 7a-tetrahydro-4, 7-methanoindene or Heptachlor m.p. 92°-94°C, stable in 0.04 Methanol-NaOH;
   d) 4, 5, 6,7, 8, 8-Hexachloro-3a, 4, 7, 7a-tetrahydro-4, 7-methanoindene or Hexachlor, m.p. 154°C (with decomposition);
   e) 1, (or 3a,) 2, 3, 4, 5, 6, 7, 8, 8-Enneachloro-2, 3, 3a, 4, 7, 7a-hexahydro-4, 7-methanoindene, Trichlor 237, Enneachlor, m.p. 122-123°C, very unstable, reactive in 0.04M ethanol-NaOH.
      (1) All the foregoing are white, crystalline solids, the first two (a, b) being chromatographically separable on aluminum oxide.
      (2) Heptachlor, 2 times as toxic as tech. chlordane for higher animals, is 4-5 times more insecticidal than tech. chlordane.
      (3) trans-chlordane (β-chlordane) is 10 times more toxic than cis-chlordane (α-chlordane), but somewhat less insecticidal than Heptachlor.
   f) The following have been separated, according to several workers:
      (1) $C_{10}H_5Cl_7$ m.p. 92-93°C (Heptachlor?)
      (2) α-$C_{10}H_6Cl_8$ m.p. 106.5-108°C (105.5-106.5°C)
      (3) β-$C_{10}H_6Cl_8$ m.p. 104.5-106°C (102-103.5°C)
      (4) α-$C_{10}H_5Cl_7$ m.p. 143-144°C
      (5) β-$C_{10}H_5Cl_7$ m.p. 86°C (Heptachlor?)
      (6) γ-$C_{10}H_5Cl_7$ m.p. 102°C
      (7) γ-$C_{10}H_6Cl_8$ m.p. 141-141.5°C
      (8) $C_{10}H_5Cl_9$ m.p. 209-211°C
   g) Five isomers of $C_{10}H_6Cl_8$ have been claimed (m.p. 101-103°C, 102-104°C, 81-84°C, 137-139°C, 73°C).

3) Formulations: As wettable powders, emulsifiable concentrates (e.g. 25-72% emulsion bases), oil solutions (e.g. 2-20% in kerosene), low to high percentage dusts (e.g. 40-70% dusts), and as technical chlordane in two grades: Refined and agricultural. Agricultural grade used where surface staining is no problem, refined grade for household insect control; both essentially equal in insecticidal capacity. All formulations are required to carry a label of caution with details appropriate to the particular formulation as prescribed in Ref. 3150.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD$_{50}$	430		807
Rat	or	LD$_{50}$	200-250	Given in olive oil.	2985
Rat	or	LD$_{50}$	250		1645
Rat	or	LD$_{50}$	500		1949
Rat	or	LD$_{50}$	750		2321
Rat	or	LD$_{50}$	470		807
Rat	or	LD$_{50}$	590	Given in cottonseed oil.	48
Rat	or	LD$_{50}$	500 +		3307
Rat	or?	MLD	150		3307
Rat	or	LD$_{50}$	457-590	As technical chlordane.	2231
Rat	or	LD$_{50}$	700	As α-chlordane.	2231
Rat	ct	LD	50	As a daily dose for 4 days.	50
Rat	ip	LD$_{50}$	200	In olive oil.	2985
Rabbit	or	LD$_{50}$	300	In olive oil.	2985
Rabbit	or	LD$_{50}$	100	In Tween 20.	2985
Rabbit	ct	LD$_{50}$	< 780	Single dose in dry form.	1952
Rabbit	ct	LD$_{50}$	20-40	Repeated, daily exposure.	1952
Rabbit	ip	LD$_{50}$	150-225		3307
Rabbit	iv	LD$_{74}$	20	In Tween 20.	2985
Rabbit	iv	LD$_{50}$	20-40		3307
Goat	or	LD$_{50}$	180		3277
Sheep	or	LD$_{50}$	500-1000		3277
Sheep	or	Toxic	80		3277
Animals	or	LD$_{50}$	80-700		353
Bass (fingerling)	medium	Toxic	0.2 ppm	Dust.	1937
Bluegill (fingerling)	medium	Toxic	0.2 ppm	Dust.	1937
Trout (larva)	medium	Disabling	5.0 ppm.	Emulsion.	595
Trout (larva)	medium	Disabling	30.0 ppm	Acetone solution.	595
Fish (most)	medium	LC	1 lb/acre	Dust.	2026
Fish (most)	medium	Survived	0.5 lb/acre	Dust.	2026

a) For man, the MLD has been estimated at between 6-60g. Ca100 mg/k has resulted in death of the human adult. 3307, 2221, 89, 3229

2) Cumulative, chronic toxicity; higher animals:

a) The liver damage, noted in animals on diets containing chlordane at 2.5 ppm, indicates a toxicity too great to warrant its use on food crops for man or animals. 1950

b) Hazardous to wildlife, notably to fish. 129, 3114, 603, 215

c) Toxic hazard at least 4 times greater than for DDT. α-Chlordane is < toxic than tech. chlordane; at 5 ppm in diet of rats showed no effect; at 150 ppm: Liver damage. 1950, 1647

d) Cumulative oral toxicity induced in short duration experiments:

Rat:	25 mg/k/day for 15 days showed no toxic signs.	3307
Rat:	50 mg/k/day after 9 days showed death of 60% of subjects.	3307
Rat:	75 mg/k weekly dose brought death in 4 months.	1645
Rat:	10 mg/k daily dose showed survival for 4 months.	1645
Rabbit:	1.7 mg/k, 42 doses over 58 days yielded no toxic signs.	3307
Dog:	5 mg/k/day, for 32-72 weeks, yielded no deaths; some liver histopathology.	3307
Dog:	660, 600 ppm in diet brought death within weeks.	1949, 407
Dog:	250 ppm in diet yielded gross signs of intoxication within 4 weeks.	1949

e) Chronic toxicity; dietary experiments of long duration:

Rat:	150 ppm, or less, 2 yr exposure: Mortality unaffected.	3307
Rat:	300 ppm, or more, 2 yr exposure: Increase of mortality above normal.	3307
Rat:	Threshold for growth inhibition: 300 ppm.	3307
Rat:	Threshold for liver enlargement (increased liver wgt.): 150 ppm.	3307
Rat:	Liver damage increasing in severity from 50 ppm and above.	3307
Rat:	Zone of no significant liver change: Below 50 ppm.	3307
Rat:	Kidney degenerative changes from 75-100 ppm and above.	3307
Dog:	Chronic toxicity detectable on diets with 5 ppm or above, exposures of 15-18 months.	407

f) Dermal toxicity:

(1) Absorbable via the unbroken skin; irritating to the skin. 2221, 89

(2) Plant workers (in chlordane manufacture), exposed to contact for several years, showed no overt intoxication, no allergic response. 2548, 3307
(3) Single dose dangerous to man: 113 g; multiple dose: 2.4 g/day. 3307
(4) Rat: Survived 25 mg/k/day for 65 days; at 50 mg/k/day for 65 days, 40% of subjects died. 3307
(5) Use of 1-1.5 gallon 2% emulsifiable concentrate on cattle every other week for 24 weeks led to no apparent injury. 3307
(6) Twice daily spraying of horses with 1.5% chlordane gave no toxic effect. 3307
(7) Four successive sprays, or 6-8 dips, in 1.5-2% emulsions, suspensions, fatal to goats, sheep, cattle; goats, cattle: Death within 2 days, sheep: Within 2 weeks. 2568
(8) Farm animals: 6 sprays of 1.5% chlordane, given 8 times at 4 day intervals, led to liver necrosis. 407
(9) Repeated cutaneous dosage, as low as 40 mg/k, is dangerous. Cattle tolerate 1-2 treatments 2% sprays, dips, at 2 week intervals, but may be killed by 3 treatments. Calves may occasionally be killed by 1% sprays. Relatively safe as to acute toxicity, hazardous in chronic effect. 1949, 2571

g) Toxicity of chlordane vapors:
(1) High vapor toxicity for mice reported. Ascribed by some to presence of unreacted hexachlorocyclopentadine and apparently confirmed. 1067, 1646
(2) Mice: Survived 25 days continuous exposure to vapor from a saturation train. 3307
(3) Rats: Exposed 8 hrs/day for 7 days to saturation train vapor, gave no toxic symptoms. 3307
(4) Rabbits, Guinea pigs, rats, mice, chickens, in room fogged with 7% chlordane: No injury. 3307
(5) Pigeons, chickens, in poorly ventilated box treated at rate of 1000 mg/ft^2 for 30-60 days, showed no overt injury. 3307

h) Toxicity of chlordane for man; two cases of fatal poisoning: 770, 89
(a) Patient I, ♀ 23 yrs: Dermal absorption by spilling over clothing unknown amount of a suspension (25 lbs chlordane, 26 lbs DDT, 39 lbs Velsicol AR 50, 10 lbs Triton).
(1) Within 40 minutes: Confusion, generalized convulsions; dead on arrival, shortly afterward, at medical office.
(2) Non-specific changes in brain, kidneys, lungs: Lungs, kidneys showed congestion, hemorrhage; brain showed congestion, edema, petechiae; liver was pale; stomach mucosa showed congestion.
(b) Patient II, ♀ 32 yrs: With suicidal intent by mouth 1/2 of 8 oz glass full of Toxichlor dust (5% chlordane, 95% talc), estimated to contain 6g chlordane (<104 mg/k body wgt), with water.
(1) Toxic dose taken at 8 P.M. (Nov. 19)
(2) At 10:30 P.M.: Vomit with blood, followed by coughing, hoarseness.
(3) Hospital admission noon of following day: Apprehensive, agitated, mouth very sore, breathing noisy, moist rales, gray exudate over gums, mouth, pharynx, tonsils, uvula, tongue, red; patient anuric.
(4) November 21: Increased pain, mouth, throat, epigastrium.
(5) November 22: Continued pain; intense anxiety; bloody stool.
(6) November 23: Palmar erythema; restlessness.
(7) November 24: Speech incoherent, irrational.
(8) November 26: Vomiting, diarrhoea; diffuse bronchopneumonia.
(9) November 27: Increasing agitation.
(10) November 28: Moaning, continuous shouting, crying; pronounced fall in blood pressure at midnight; muscle twitching; at 2:15 A.M. (November 29): Tonic, clonic, convulsions (generalized) for 10 minutes; shorter convulsions until death at 8:30 A.M. ca. 9 1/2 days after toxic dose, with supportive, symptomatic treatment throughout.
(11) Pathology: Conjunctival hemorrhage, gum ulceration, epiglottis ulcerated. Lungs: Thin exudate, bronchopneumonia; Heart: Ventricles dilated, myocardium flabby; brain: No gross abnormalities; liver: Congested areas; spleen: Malpighian corpuscles indistinct; kidneys: Pale, flabby; cortex pale, swollen; pyramids red, congested. Microscopic: Myocardium petechial, congested; kidneys: Heme casts in distal collecting tubules of nephrons; brain: Gliosis in basal ganglia.
(c) Summary of certain human poisonings involving chlordane:

Circumstance	Exposure Route	Exposed To	Dose	Results	
Agriculture:					
Exterminator	Inhalation, ct	Spray	—	Recovered.	441
Unspecified	Inhalation, ct	Spray	—	Recovered.	441
Nurseryman	Inhalation, ct	?	—	Recovered.	441
Field worker	Inhalation, ct.	Spray	—	Recovered.	441
Industry:					
Formulator	ct	Chlordane-DDT solution	> 100 cc	Death.	770
Home:					
Adult ♂	Inhalation, ct	Spray	—	Mild poisoning.	3229
Adult ♀ (suicide)	or	5% Powder	ca 104 mg/k	Death.	770
Adult ♂	or	Oil solution	60 cc	Moderate poisoning.	1747
Student 18 yr old	Inhalation	3% Spray	—	Death.	3229
Student 18 yr old	or	40% Oil solution	32 mg/k	Severe poisoning.	867
Child 3 yr old	or	2% Solution	30-40 mg/k	Severe poisoning.	1522
Infant 10 mo	ct	2% Spray	"small amt"	Mild poisoning.	1522
Child 15 mo	or	50% Wettable pwdr	10 mg/k	Severe poisoning.	1970
Adult ♂	or	2% Oil solution	2-4 g	Death.	3229
Adult ♂	ct	2% Oil solution	500 cc	Death.	1906

3) Pharmacological, pharmacodynamic, physiological, biochemical, etc.:
   - a) Pharmacological characterization handicapped because commercial product is not a chemical entity, but a variable mixture of chlorinated hydrocarbons. 3229, 89
     - (1) One of the more hazardous common insecticides, with definite residual properties despite a relatively high vapor pressure.
     - (2) Readily absorbed by the skin, and other portals—gastrointestinal, respiratory.
     - (3) More toxic, dermally, than DDT; lipophilic, and easily absorbed, neat or in solution. Dry formulations do not minimize the skin hazard, the substance being an oily liquid. Irritant to skin. Wettable powders have relatively high toxicity and hazards of repeated exposure impose caution on use in waxes, polishes, etc.
     - (4) Too toxic for formulation as a louse powder for man. Least acceptable insecticide for farm animal dips, the margin of safety between pest control and animal toxicity being too narrow. May be absorbed from any type of formulation, although physical state and nature of solvent may influence rate of absorption.
   - b) A central nervous stimulant; the exact mode of action is unknown. Poisoned animals show marked loss of appetite at same time as neurological symptoms, namely: Hyperexcitability and tremors. 3307, 1645
   - c) Distribution in the tissues obscure. There is evidence of fat storage, but disappearance is rapid after exposure is ended. May be stored as an epoxide. 706, 2571
     - (1) Acidic, chlorine-containing products (isolated from rabbit urine) suggest metabolic detoxification. 2987
     - (2) A substance, toxic to young rats, is secreted by lactating rats fed 150 ppm chlordane in diet. 3229
   - d) Symptoms are DDT-like, but of longer duration with chlordane, and are referrable to the CNS, for instance irritability, salivation, tremors, convulsions. Sodium amytal partly controls. 3307, 3229, 353
     - (1) In rats: Anorexia, hyperexcitability, tremors. 1645
     - (2) In cattle: Ataxia, blindness (peculiar to chlordane, absent in DDT intoxication) pain, convulsions (with opisthotonus and prolonged limb paddling) cyanosis leading, in fatal cases, to agonized death. 2568
     - (3) In man: (See preceding account of 2 human fatalities). Nausea, vomiting, diarrhea, abdominal pain (oral, toxic doses). Blurred vision, cough, ataxia, confusion, delirium, mania noted following inhalation, skin absorption of toxic amounts. Acute signs as early as 45 minutes after ingestion; death possible within 24 hrs, frequent between 48-96 hrs, but may be long delayed (9 1/2 days in one case) following a single oral dose. 3229
     - (4) Chronic intoxication may be marked by anorexia, weight loss, skin irritation, liver damage, protracted inanition. Albuminuria, before death, may be the only objective sign of cumulative intoxication; disturbances of CNS, especially the optic nerve.
     - (5) Chlordane feeding to dogs: Chlordane as wettable powder 50% active ingredient: 203

Dosage (mg/k) active	Total given (mg)	Estimated Total active ingred. (mg)	Sex	Result
200	7724.0	3862	♂	Clonic spasms in 12 hrs.
225	5931.1	2065.2	♀	No effect.
250	5110.0	2555	♀	Slowed respiration.
300	11586.0	5793	♂	Clonic spasms, tremors in 4 hrs.
400	10544.0	5272	♀	Tremors, salivation convulsions, blind.
500	10220.0	5110	♀	Tremors, convulsions, prostration.
700	6356.0	3178	♂	No effect.

Chlordane feeding to sheep:

Sheep 78 lb wgt 2 g/k chlordane showed severe respiratory, nervous symptoms in 16 hrs; death in 48 hrs. 3277
Sheep 123 lb wgt 1 g/k chlordane showed severe respiratory, nervous symptoms in 16 hrs; death in 48 hrs.
Sheep 103 lb wgt 0.5 g/k chlordane showed incoordination, nervousness, partial blindness; recovery in 5-6 days.

   - e) Pathology:
     - (1) Pathology is entirely non-specific. Chronically-poisoned animals show degenerative liver and kidney changes. Pathology, in man, resembles that in poisoned animals (vide supra account of two fatal human cases). 3307, 50
     - (2) In rat: Edema, congestion, hemorrhage of lungs; pitting of kidneys; liver necrosis. 1949, 1645
     - (3) In cattle, other livestock: Petechial hemorrhages, large and small, of intestines, heart and elsewhere; congestion of brain and cord; swelling and y degeneration of liver (suggestive of chloroform, organic chlorides, damage). 2568, 2321

4) Residue hazard:
   - a) Volatility of chlordane tends to minimize the hazard, which, in two weeks after application, becomes negligible. 353
     - (1) Applied, at 1 lb/acre, to alfalfa residue declined from 18 to 3 ppm in 15 days. 1126
     - (2) Applied, at 2.5 lbs/acre, to alfalfa residue declined from 24 to 2 ppm in 30 days. 1126
     - (3) Clover, treated at rate of 1 lb/acre, showed no harmful effect when fed to ewes, lambs; alfalfa, treated at 1 lb/acre, no harm to yearling heifers; pasture, treated at 4 lbs/acre, no harm to sheep grazed thereon for 3 weeks. 3277

5) Phytotoxicity:
   - a) Not markedly phytotoxic at properly applied insecticidal concentrations, but may injure some plants at high strength. 129, 1953
   - b) Accumulates in the soil on repeated application at normal levels (6-10 lbs/acre). A more hazardous soil contaminant than toxaphene. 294, 129, 353

(1) Stable in the soil, fungicidal. Depresses seed germination. 129, 663
c) Not toxic to apple foliage; may injure spring leaves of cherry, plum, peach. 0.1% suspension yielded 1606, 482
defoliation, bud injury, possible fruit damage to plum. Dusts may do transient damage to some squash 1769
varieties. Tomato transplants may be "burned", the danger being enhanced by dew.
d) Greenhouse plants:
(1) Leaf fall in Abutilon; damage to Poinsettia. 835
e) At 10 lbs per acre: No effect on cereals, vegetables, soybeans, annual flowering ornamentals, grasses. 1023
Seedling growth, however, may be retarded without apparent pathology. 663
f) At 20 lbs/acre: Harmless to tobacco, cotton, soybean, cowpeas, corn, rye; at 25 lbs/acre: Harmless to wide 294
variety of grasses, but 40-80 lbs/acre may temporarily damage lawns and at 200 lbs per acre (greenhouse 2778
tests) is more toxic to sorghum than to most other grasses. At 100 lbs per acre, turf plants, e.g. clover,
bent grasses, were damaged.
g) At 25 lbs/acre: Lima beans showed stunting, chlorosis. 2304
h) At 20-25 lbs/acre: Has injured the germination of beans, beets, tomatoes, cucurbits, and 100 lbs per acre 294
does serious damage; many vegetables tolerated 20 lbs per acre. Lima bean, corn, cabbage family germination unaffected by 100 lbs per acre. Five lbs per acre injured growth of sensitive squash varieties, others stood 25 lbs per acre. After emergence from soil some vegetables are harmed by 20 lbs per acre, others stand 100 lbs/acre. Cucumbers, muskmelons, honey dew melons, squash, are in general highly sensitive.
i) At 50 lbs per acre, applied to soil, germination of tobacco was completely suppressed; cabbage, lettuce, 1769
tomato unaffected.
j) At 100-500 lbs per acre nitrate formation by soil microorganisms was depressed. 15-20% of heavy dosages 294
applied to soil disappear per year.
k) Not phytotoxic to 20 species of conifers, in dosages to 100 lbs per acre. Does not harm Norway pine seed- 2838
lings in sand culture.

6) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Agrotis orthogonia (larva)	Contact	L Deposit$_{50}$	18 µg/cm^2		350
Anopheles quadrimaculatus (adult) ♂	Topical	LD$_{50}$	0.105 µg/insect	In ethanol solution; 4 day old adults.	2051
Anopheles quadrimaculatus (adult) ♀	Topical	LD$_{50}$	0.24 µg/insect	" " "	2051
Anopheles quadrimaculatus (adult) ♂	Topical	LD$_{90}$	0.19 µg/insect	" " "	2051
Anopheles quadrimaculatus (adult) ♀	Topical	LD$_{90}$	0.46 µg/insect	" " "	2051
Anthonomus grandis (adult)	Contact, or	LD$_{50}$	10.1 lb/acre	Insects on dusted food plants.	2276
Anthonomus grandis (adult)	Fumig	LC$_{50}$	21 mg/l		2276
Apis mellifera (adult).	or	LD$_{50}$	1.2 µg/insect		910
Anasa tristis (adult)	Topical	approx LD$_{90}$ 72 hr	512 µg/g		3376
Blabera fusca	inj	MLD < 7 days	8 µg/g	In acetone-triton solution.	1986
Blabera fusca	inj	Maximum Tolerated	14 µg/g	" "	1986
Blattella germanica	Direct Spray	L Deposit$_{50}$	1.7 µg/cm^2		356
B. germanica	Direct Dust	L Deposit$_{50}$	2.0 µg/cm^2		356
B. germanica	Environment Dusted	L Deposit$_{50}$	0.6 µg/cm^2		356
B. germanica (adult) ♀	Topical	LD$_{50}$ 48 hr	2.3 µg/insect	Non-R, laboratory strain.	1012
B. germanica (adult) ♀	Topical	LD$_{50}$ 48 hr	4.1 µg/insect	DDT-R strain.	1012
B. germanica (adult) ♀	Topical	LD$_{50}$ 48 hr	250.0 µg/insect	Chlordane-R strain.	1012
B. germanica (adult) ♀	inj	LD$_{50}$	81.29 µg/g	Non-R, laboratory strain.	431
B. germanica (adult) ♀	inj	LD$_{90}$	144.27 µg/g	" "	431
B. germanica (adult) ♀	inj	LD$_{50}$	1117.5 µg/g	Chlordane-R (Corpus Christi) strain.	431
B. germanica (adult) ♀	inj	LD$_{90}$	4648.8 µg/g	" " "	431
Choristoneura fumiferana (larva)	Contact	L Deposit$_{50}$	140 µg/cm^2		350
Chrysops discalis (adult)	Topical	LD$_{50}$ (estimate)	0.06 mg/fly		2707
Chrysops discalis (adult)	Topical	LD$_{90}$	0.65 mg/fly		2707
Ephestia kuehniella (larva)	Medium	LC$_{50}$	36 ppm	Mixed with whole grain.	353
Melanoplus differentialis	Topical	LD$_{50}$	9.8, 16.3 µg/g	In solution, dioxane, acetone, ethanol.	3266
M. differentialis	or	LD$_{50}$	12.0, 21.8 µg/g	As deposit on leaves.	3266
M. differentialis (1st, 2nd instar)	Contact Spray	LC$_{50}$	0.49 lb/acre	Emulsion from miscible concentrate.	1102
Melolontha melolontha	Contact	LD$_{50}$ 5 da	9 µg/insect		3184
Melolontha melolontha	Contact	LD$_{80}$ 5 da	20 µg/insect		3184
Musca domestica (larva)	Medium	LC$_{50}$	28 ppm	Incorporated in rearing medium.	351
Musca domestica (larva)	Medium	LC$_{100}$ ca	15 mg/k medium	Laboratory tests.	1326
Musca domestica (larva)	Medium	LC$_{75}$	2 mg/k medium	"	1326
Musca domestica (larva)	Medium	LC$_{50}$	1450 (1100-1900) ppm	95% confidence limit; as measured by pupal emergence.	666
Musca domestica (adult)	Topical	LD$_{50}$	4.0 µg/g	Technical chlordane.	2231
Musca domestica (adult)	Topical	LD$_{50}$ 24 hr	0.12 µg/fly	At 60°F; laboratory non-R strain.	371
Musca domestica (adult)	Contact Spray	LC$_{50}$ 24 hr	0.25 mg/cc	Turntable method; 0 KD in 10 min.	2033
Musca domestica (adult)	Vapor	LT$_{50}$*	33 minutes	Non-DDT R strain; *=time for 50% kill at vapor saturation.	3320
Musca domestica (adult)	Vapor	LT$_{50}$*	69 minutes	DDT-R, Orlando #1 strain; *=time for 50% kill at vapor saturation.	3320
Musca domestica (adult)	Vapor	LT$_{50}$*	347 minutes	LDD strain; *=time for 50% kill at vapor saturation.	3320
Musca domestica (adult)	Vapor	LT$_{50}$*	380 minutes	Ballard strain, " "	3320
Oncopeltus fasciatus	Topical	LD$_{50}$	145 µg/g	Technical chlordane.	2231
Oncopeltus fasciatus	Topical	LD$_{50}$	459 µg/g	α -Chlordane.	2231
Oncopeltus fasciatus	Topical	LD$_{50}$	47 µg/g	β -Chlordane.	2231
Periplaneta americana	Topical	LD$_{50}$	10 µg/g	Technical chlordane.	1757
Periplaneta americana (adult) ♂	inj	LD$_{50}$ 96 hr	26 µg/g	Solution in xylene 10 pts, acetone 10 pts, ethanol 5 pts, deobase 75 pts.	558
Periplaneta americana (adult) ♀	inj	LD$_{50}$ 96 hr	52 µg/g	" " "	558
Prodenia eridania (larva, 12 mg wgt)	Vapor	96.3% kill	at saturation	2 day exposure at 24°-25°C yielded 96.3% kill.	3017
Prodenia eridania (larva, 700 mg wgt)				2% Average kill at 2 day contact with deposit 0.55 mg/cm^2.	3017
Prodenia eridania (larva, 700 mg wgt)	or	LD$_{50}$	130 µg/g	Administered by leaf sandwich method.	3017
Sitophilus spp,	Medium	LC$_{50}$	1.3 ppm	Mixed with whole grain.	353
Tribolium spp.	Medium	LC$_{50}$	0.2 ppm	Mixed with whole grain.	353

a) Generalization of comparative toxicity for insects; chlordane and some other chlorinated hydrocarbons: 3017
   (1) Oral route: Lindane > DDT > chlordane.
   (2) Contact route: DDT > lindane > chlordane.
   (3) Fumigant: Chlordane > lindane > DDT.

b) Data on the comparative toxicity of chlordane and other insecticides:
   (1) Sex differences in susceptibility: Vs. Periplaneta americana (adults): 558
   route: Injection; vehicle: Xylene 10 parts, acetone 10, Deobase 75, ethanol 5:

Insecticide	♂ LD_{50} 96 hr (μg/g)	♀ LD_{50} 96 hr (μg/g)	$\frac{LD_{50}}{LD_{50}\,♂}$ (Ratio)
Chlordane	26.0	52.0	2
Lindane	0.8	4.4	5.5
Dieldrin	1.0	5.0	5
DDT	4.5	20.0	4.4
Toxaphene	25.0	80.0	3.2
Methoxychlor	7.0	18.0	2.5

   (2) Vs. Blattella germanica (adult): 356, 2357

Insecticide	Lethal Deposit $_{50}$ (μg/cm²)		
	Direct Spray	Direct Dust	Environmental Dust
Chlordane	1.7	2.0	0.6
Lindane	2.8	0.8	0.2
DDT	40.0	15.0	2.5
Sodium fluoride	—	130.0	40.0

   (3) Vs. Blattella germanica (adult); by dust settling chamber method, 8 minute run on the dusted surface; dust diluent: Pyrophyllite; 5 roaches/test, 10 tests: 1234

Insecticide	% Active Ingredient	% Mortality (♂)	Survival Time (♂) (Hrs)	% Mortality (♀)	Survival Time (♀) (Hrs)
Chlordane	2	100	40.6	98	68.8
	1	100	52.8	82	84.5
" + 50% pyrethrum marc	1	100	54.7	46	80
BHC	1	100	33.3	100	55.3
" + 75% pyrethrum marc	1	100	28.0	100	52.4
" (Merck)	1	100	31.1	100	47.8
" "	0.5	100	38.3	100	65.9
" + 50% pyrethrum marc	0.5	100	27.7	98	62.1
" (DuPont)	1	66	52.8	20	70.0
Toxaphene	5	100	29.3	100	40.1
"	10	100	15.0	100	22.3
Sabadilla (McConnon)	10	98	28.7	75	52.2
" "	50	100	11.8	100	22.7
Sabadilla + 50% pyrethrum marc	10	100	33.9	57	54.8
" + 50% boric acid	10	100	64.0	40	73.7
" + 50% sulfur	10	76	45	12	—
Sodium fluosilicate	25	100	45.6	49	77.0
Sodium fluoride	10	92	34.6	48	63.5
Sodium fluoroacetate	1	100	19.7	90	42.5
Pyrethrum marc (Powell)	10	0		0	

   (4) Vs. Blabera fusca; by injection in acetone-triton solution: 1986

Insecticide	MLD (μg/g) (in < 7 da)	Maximum Tolerated Dose (μg/g) (7 da)
Chlordane	8	14
Heptachlor	1.6	5
Aldrin	1.3	2.6
Isodrin	1.5	2.7
Dieldrin	1.5	2.6
Endrin	1.3	2.5
Acetone-Triton control	454	1388

   (5) Vs. Periplaneta americana (adult); comparative effectiveness of insecticides in urea-formaldehyde wall surface coatings; 50% insecticide incorporated, as based on dry weight of coating: 267

Insecticide	Time for 50% KD (hrs)	Time for 100% KD (hrs)
Chlordane	15	18
DDT	24	48
Lindane	1	1.5
Toxaphene	> 48	—
DDD	> 48	—

(6) Vs. Prodenia eridania (larva); small larvae = 12 mg wgt, large = 700 mg wgt: 3017

Insecticide	Fumigant Action Average Kill % (2 days) Small Larvae	LD$_{50}$ (mg/g) Oral; Large Larvae	Contact Action Deposit (mg/cm^2)	Contact Action Average Kill % (2 days) (Large Larvae)
Chlordane	96.3	0.13	0.55	2
Lindane	35.0	0.031	0.58	32
DDT	15.0	0.031	0.53	40
Lead arsenate	—	0.29	—	—
Control	0			0

(7) Vs. Sitophilus, Ephestia, Tribolium, stored products insects. Insecticides mixed with grain: 353

Insecticide	Sitophilus LC$_{50}$ (ppm)	Ephestia LC$_{50}$ (ppm)	Tribolium LC$_{50}$ (ppm)
Chlordane	1.3	36	0.2
DDT	16	860	16
Lindane	0.1	10	3
Hexachloropropene	450	4	10

(8) Vs. Anopheles quadrimaculatus; 4 day old adults, topical application of insecticides in ethanol solution: 2051

Insecticide	LD$_{50}$ (μg/insect)		LD$_{90}$ (μg/insect)		Relative Effectiveness (DDT=1.0) at LD$_{50}$		Relative Effectiveness (DDT=1.0) at LD$_{90}$	
	(♂♂)	(♀♀)	(♂♂)	(♀♀)	(♂♂)	(♀♀)	(♂♂)	(♀♀)
Chlordane	0.105	0.24	0.19	0.46	0.19	0.28	0.24	0.28
p′p′-DDT	0.020	0.066	0.045	0.13	1.0	1.0	1.0	1.0
p′p′-TDE	0.041	0.1	0.098	0.22	0.49	0.66	0.46	0.59
Methoxychlor (tech)	0.035	0.1	0.078	0.22	0.57	0.66	0.58	0.59
Dieldrin	0.009	0.023	0.022	0.048	2.2	2.9	2.0	2.7
Lindane	0.0085	0.011	0.032	0.042	2.4	6.0	1.4	3.1
Toxaphene	0.15	0.29	0.29	0.5	0.13	0.23	0.16	0.26
Malathion	0.0087	0.0095	0.019	0.022	2.3	7.0	2.4	5.9
Allethrin	0.0029	0.008	0.013	0.041	6.9	8.3	3.5	3.2

(9) Vs. Chrysops discalis (adult); topical application: 2707

Insecticide	LD$_{50}$ (estimate) μg/fly	LD$_{90}$ μg/fly
Chlordane	60	650
Lindane	4	35
Endrin	9	80
DDT	20	250
Dieldrin	20	950
Methoxychlor	30	90
Aldrin	40	170
Heptachlor	40	200
EPN	48	120
Isodrin	60	170
Bayer 22/190 (Chlorthion)	65	420
Diazinon	90	360
3-Chloro-4-methyl umbelliferone, 0,0-diethyl thiophosphate	90	910
Q-137 (Perthane)	120	400
Malathion	130	330
Toxaphene	180	480

(10) Vs. Musca domestica (adult); contact sprays applied by turntable modification of the Peet-Grady method: 2033

Insecticide	Spray Concentration (mg/cc) (to give 50% kill in 24 hrs.)	% KD In 10 Minutes (at the conc. for 50% kill in 24 hrs)
Chlordane	0.25	0
Dieldrin	.017	0
Parathion	.02	0
Methyl parathion	.025	0
Lindane	.046	0
Heptachlor	.052	0
Aldrin	.056	0
TEPP	.069	ca 70%
DDT	.35	0
Malathion	.48	0
Toxaphene	.68	0
Tetrapropyl dithiopyrophosphate	0.69	0
Dilan	0.72	ca 30%

(10) Vs. *Musca domestica* (adult); contact sprays applied by turntable modification of the Peet-Grady method: 2033

Insecticide	Spray Concentration (mg/cc) (to give 50% kill in 24 hrs.)	% KD In 10 Minutes (at the conc. for 50% kill in 24 hrs)
Isolan (G-23611)	1.15	100
Allethrin	1.5	100
Pyrolan	5.5	100

(11) Vs. *Musca domestica* (adult); comparative effectiveness of insecticides in urea-formaldehyde and other wall surface coatings; 20% insecticide incorporated in coating on dry weight basis: 267

Insecticide	Vehicle	Time for 50% KD (Minutes)		
		Initial Test	After Specified Interval*	Interval Between Tests (Wks)
Chlordane	Urea-formaldehyde	60	41	7
DDT	" "	16	10	28
Lindane	" "	13	16	6
Toxaphene	" "	48	35	12
DDD	" "	28	25	17
Pyrethrum	" "	18	2, 11, 23, 52	8, 14, 15, 17 days
Chlordane	nitro-cellulose	76	28	30
DDT	" "	60	17	35
Lindane	" "	39	20	30
Toxaphene	" "	55	26	12
Chlordane	polymerized diolefins	71	29	30
DDT	" "	21	32	6
Lindane	" "	20	23	6

*Namely the interval named in rightmost column.

(12) Vs. *Musca domestica* (larvae); insecticides incorporated in rearing medium; laboratory tests of control achieved. (Field results far less encouraging): 1326 666

Insecticide	% Mortality [Ref. 1326] (Mg Active Ingredient/K Medium)						LC$_{50}$* [Ref. 666]
	50 mg	20 mg	15 mg	10 mg	5 mg	2 mg	
Chlordane	—	—	100	—	—	75	1450 ppm (1100-1900) = .95 Fiducial limits
DDT	100	—	—	—	—	—	2300 ppm (1600-3300) = " " "
Methoxychlor	25	—	—	—	—	—	— — " " "
Toxaphene	100	100	—	100	75	0	— — " " "
Lindane	—	99.5	—	60	—	—	— — " " "
Aldrin	—	—	100	100	100	97.5	430 ppm (340-595) = " " "
Dieldrin	—	100	—	100	100	94	450 ppm (355-595) = " " "
Endrin	—	—	—	—	—	—	125 ppm (100-160) = " " "
Heptachlor	—	100	—	—	100	90	— —
Dilan	99.5	100	—	100	5	—	— —

*Measured by % emerging from pupa in experimental culture compared with control.

(13) Vs. *Melanoplus differentialis*; comparative toxicity, various insecticides, methods: 3267, 1102

Insecticide (Laboratory tests)	LD$_{50}$ (μg/g), Contact* (adult insects) [Ref. 3267]	LD$_{50}$ (μg/g), Oral)** (adult insects) [Ref. 3267]	LD$_{50}$ (lbs/acre), Contact Emulsion Sprays;*** 1st, 2nd Instar Nymphs. [Ref. 1102]
Chlordane	16.3, 9.8	21.8, 12.0	0.49
DDT	> 3300, 9380	> 1350, 2579, 1170****	—
Toxaphene	73.9, 61.0	75.0, 91.5	0.91
Lindane (γ-BHC)	1.6, 3.4	6.6, 6.7	0.08
BHC	—	—	0.04
Heptachlor	2.6, 1.6	6.0, 4.4	—
Aldrin	1.8	2.3	0.04
Dieldrin	1.4	3.7	0.03
Parathion	0.7, 0.8	6.0, 8.9	0.05
TEPP	4.4	—	—
HETP	18.4	—	—

*Solutions in dioxane, acetone, ethanol; **Deposit on leaves; ***From miscible oil concentrates; ****Colloidal suspension, directly applied to mouth parts.

(14) Vs. Sphenarium purpurascens; cornfield tests: 307

Insecticide	Concentration	Active Ingredient (lbs/acre)	% Mortality 12 hrs	% Mortality 24 hrs
Chlordane	2.5% dust	0.95	32 (27-39)	46.6 (41-54)
"	5% "	1.8	49.6 (39-62)	63.8 (50-77)
Dieldrin	1% "	0.35	74.2 (68-80)	98.2 (96-100)
"	2.5% "	0.88	89.8 (87-93)	99.8 (99-100)
Aldrin	1% "	0.32	77.8 (69-88)	97.8 (95-100)
"	2.5% "	0.82	88.6 (83-96)	99.6 (99-100)
BHC	1% "	0.36	86.6 (78-92)	94.2 (90-97)
"	2.5% "	0.85	93 (89-98)	97 (93-100)
Isodrin	0.5% spray	0.43	83.2 (81-82)	91.4 (80-86)
Parathion	0.5% dust	0.16	43.6 (36-51)	69.4 (61-80)
"	1% "	0.35	66.8 (59-80)	76 (69-84)
Toxaphene	5% "	1.74	26.8 (18-36)	53 (46-60)
"	10% "	3.6	40.4 (36-47)	61.4 (55-69)
Endrin	0.5% spray	0.36	32.8 (24-40)	47.6 (43-59)

(15) Vs. Melolontha melolontha: (DDT not efficacious.) 3184

Insecticide	Contact (μg/Insect)		Relative Toxicity	
	LD_{50} (5 day)	LD_{80} (5 day)	At LD_{50}	At LD_{80}
Chlordane	9	20	0.08	0.12
BHC (tech)	0.7	2.5	1.0	1.0 (Standard)
Dieldrin	1.6	5	0.4	0.5
Aldrin	2.7	> 6	0.25	< 0.4
Toxaphene	ca 7	ca 20	ca 0.1	ca 0.12

(16) Vs. Anasa tristis (adult); rates of action (topical application) insecticides at the lowest dosage yielding a mortality of 90% or more: 3376

Insecticide	μg/g Insect	% Mortality At			
		12 hrs	24 hrs	48 hrs	72 hrs
Chlordane	512	—	6.7	73.3	90.0
Parathion	6	3.3	33.3	76.7	90.0
Lindane	64	—	80.0	100	100
Aldrin	64	—	23.3	76.7	93.3
Endrin	128	6.7	20.0	86.7	100
EPN	128	10	26.7	76.7	100
Heptachlor	128	10	50.0	80.0	90.0
Isodrin	128	0	10.0	63.3	90.0
Dieldrin	256	0	70.0	96.7	100

(17) Vs. Leptinotarsa decemlineata (3rd instar): 1986

Insecticide	As Sprays				As Dusts			
			% Survival At				% Survival At	
	g/100 l	g/hectare	24 hrs	48 hrs	g/k	g/hectare	24 hrs	48 hrs
Chlordane	50	316	34	24	50	1485	1	0
Heptachlor	10	76	100	80	50	1228	8	4
"	20	118	66	26	22	624	38	12
"	—	—	—	—	12.5	291	57	37
Aldrin	10	76	88	72	12.5	260	2	0
"	20	136	32	22	6	184	52	24
"	—	—	—	—	3	92	66	48
Isodrin	10	65	46	2	25	604	0	0
"	—	—	—	—	12.5	395	20	0
"	—	—	—	—	6	175	26	0
"	—	—	—	—	3	97	62	46
Dieldrin	10	67	7	0	12.5	354	0	0
"	—	—	—	—	6	164	8	0
"	—	—	—	—	3	85	18	0
Endrin	10	72	2	0	25	686	0	0
"	—	—	—	—	12.5	468	12	0
"	—	—	—	—	6	184	22	0
"	—	—	—	—	3	82	78	48

(18) Vs. Choristoneura fumiferana, Heliothis ononis, Agrotis orthogonia (Lepidoptera): 350

Insecticide	Lethal $Deposit_{50}$ ($\mu g/cm^2$) For		
	Choristoneura	Heliothis	Agrotis
Chlordane	140	Ineffective	18
DDT	0.3	7	80
Lindane	1.9	23	5.5

(18) Vs. Choristoneura fumiferana, Heliothis ononis, Agrotis orthogonia (Lepidoptera): 350

Insecticide	Lethal Deposit$_{50}$ ($\mu g/cm^2$) For		
	Choristoneura	Heliothis	Agrotis
DNOC	4.0	16	7.5
Nicotine	42	400	Ineffective
Pyrethrins	0.05	4	8.2

(19) Vs. Macrosiphum pisi; speed of toxic action against. As dusts applied by dusting tower method to infested broad bean plants, (Vicia faba). Dust diluent = talc: 520

Insecticide	Dust Concentration	Temp. (°F)	Time for (Hrs: Mins)	
			50% Kill	98% Kill
Chlordane	5%	72	9 : 24	18 : 8
Toxaphene	5%	72	13 : 20	19 : 1
EPN	.86%	74	5 : 26	8 : 6
Dieldrin	1%	75	4 : 7	6 : 43
Aldrin	1%	75	3 : 44	7 : 32
TDE	5%	72	2 : 34	4 : 35
Methoxychlor	10%	75	2 : 1	5 : 34
Parathion	1%	70	1 : 8	1 : 43
Parathion	2%	70	1 : 21	1 : 53
DDT (mixture)	5%	72	0 : 57	1 : 45
Lindane	1%	72	0 : 56	1 : 54
Rotenone (5% rotenone 10% other extractives)	5%	72	0 : 47	1 : 23
TEPP	.18%	74	0 : 20	0 : 56
Nicotine	1%	72	0 : 15	1 : 12
Nicotine	3%	72	0 : 12	0 : 50
Talc (Control)		67-72	13 : 28	23 : 51

(20) Vs. Anthonomus grandis and other cotton insects: 2276

Insecticide Vs. Anthonomus grandis	LD$_{50}$ lb/acre (Active Ingred.) Combined Contact, Stomach Action, Cotton Plant Dusted	LD$_{50}$ (lb/acre active) Contact Action Insects Dusted	LC$_{50}$ (mg active/l) (Fumigant Action)
Chlordane	10.1		21.9
Dieldrin	0.9	2.7	16.6
Aldrin	1.1	6.6	12.9
BHC (tech)	1.0	3.7	47.6
Toxaphene	6.4		
DDT	9.1		
Prolan (tech)	11.4		
Bulan (tech)	16.7		

Vs. Anthonomus, rated moderately effective; Vs. Aphis, slightly effective; Vs. Nezara, slightly effective; Vs. Psallus, slightly effective; Vs. Heliothis, slightly effective; Vs. Alabama, slightly effective. 353

(21) Vs. various curculionids; comparative effectiveness, chlordane and others:

Chalcodermes aeneus	Toxaphene > DDT > Chlordane > BHC	3280
Cylas formicaria	BHC = toxaphene > DDT	561
Hylastinus obscurus	BHC > chlordane > DDT	2111
Hypera postica	Dieldrin > Chlordane > toxaphene > DDT	1447
Brachyrhinus ligustici	Chlordane > toxaphene > DDT	1312
Trichobaris mucorea	BHC > chlordane = DDT	3367
Conotrachelus nenuphar	Parathion > aldrin > dieldrin > chlordane > BHC	517

(22) Chlordane compared with other insecticides when tested by bioassay using the brine shrimp, Artemia salina (Crustacea): 2251

(a) Test method: Time required for adult Artemia to sink to bottom of a water column through failure of swimming movements.

(b) Insecticides in acetone solution.

Insecticide	Time (Minutes To Sink At)		
	1 ppm	0.1 ppm	0.01 ppm
Chlordane	60-120	120-135	120-180
Methoxychlor	45-60	45-60	45-60
Lindane	45-60	60-120	60-120
Toxaphene	45-60	90-120	18 (hr)
DDT	60	60	60-120
Acetone control 1 : 100	24-48 hrs		
H_2O control	26-50 hrs		

7) Resistance of certain insect strains (biotypes or "populations") to chlordane; comparative data:

a) Resistance to chlordane has been shown by some insect species and "populations" subjected to selection by exposure.

b) DDT resistance, in certain "populations" subjected to selection, has been accompanied in some species, by enhanced resistance ("cross resistance") to chlordane and other insecticides. Chlordane-R strains have revealed "cross resistance" to other insecticides.

c) Toxicity of chlordane for Blattella germanica, chlordane-R and chlordane non-R biotypes; applied as aqueous suspensions of acetone—EMCOL, H65A solutions; topical application by dipping of adult insects: 1260

Biotype and Sex	LC_{50} (cc/l)	LC_{90} (cc/l)	Degree of Resistance* At LC_{50}	Degree of Resistance* At LC_{90}
Chlordane non-R ♂	0.0041	0.0192	1.0	1.0
Chlordane non-R ♀	.0117	.04	1.0	1.0
Chlordane-R ♂	.340	1.5	84.1	78.1
Chlordane-R ♀	3.550	10.7	303.4	251.8

* $\frac{LC_{50}\ \text{R-biotype}}{LC_{50}\ \text{non-R biotype}}$, $\frac{LC_{90}\ \text{R-biotype}}{LC_{90}\ \text{non-R biotype}}$

(1) Toxicity of chlordane and other insecticides for the chlordane non-R, and chlordane-R (Corpus Christi) strains, of Blattella germanica; adult ♀♀ tested by injection: 431

Insecticide	Non-R		Chlordane-R		Degree of Resistance	
	LD_{50} (µg/g)	LD_{90} (µg/g)	LD_{50} (µg/g)	LD_{90} (µg/g)	$\frac{LD_{50}\ \text{R strain}}{LD_{50}\ \text{non-R}}$	$\frac{LD_{90}\ \text{R strain}}{LD_{90}\ \text{non-R}}$
Chlordane	81.29	144.27	1117.5	4648.8	13.76	32.22
Aldrin	26.46	70.06	127.61	1113.6	4.82	15.89
Dieldrin	6.59	17.35	68.37	502.49	10.37	28.54
Heptachlor	9.07	19.85	174.21	1509.3	19.21	76.04
Lindane	1.01	2.57	23.13	75.02	22.72	29.19

(2) Comparative toxicities of chlordane and 2 other insecticides for non-R and chlordane-R strains Blattella germanica; Method: Dipping; LD_{50}, LD_{90} expressed as cc insecticide/l for chlordane and TEPP and for lindane as g/l: 1259

Insecticide	Sex	Non-R		Chlordane-R		Order of Resistance	
		LD_{50}	LD_{90}	LD_{50}	LD_{90}	At LD_{50}	At LD_{90}
Chlordane	♂	0.034	0.0063	0.38	2.1	111.7	333.3
Chlordane	♀	.0165	.0476	4.55	14.87	275.7	312.3
Lindane	♂	.0103	.0155	.0595	.076	5.7	4.9
Lindane	♀	.0242	.0430	.094	.185	3.8	4.3
TEPP	♂	.0575	.11	.112	.165	1.9	1.5
TEPP	♀	.153	.395	.265	.512	1.7	1.2

(3) Comparative toxicities, various insecticides, to resistant (R) and non-resistant (non-R) strains, Blattella germanica; method = topical application to adult ♀ insects: 1012

Insecticide	LD_{50} 48 hr (µg/insect) Non-R strain	LD_{50} 48 hr (µg/insect) DDT-R strain	Degree Resistance DDT-R strain	LD_{50} 48 hr (µg/insect) Chlordane-R strain	Degree Resistance Chlordane-R strain
Chlordane	2.3	4.1	1.8	250.0	108.6
DDT	13.5	25.0	1.9	19.0	1.4
Dieldrin	0.5	0.62	1.2	34.0	68
Diazinon	0.33	0.78	2.4	0.4	1.2
Allethrin (synergized)	0.76	1.3	1.7	1.0	1.3

(4) Relative toxicity of several insecticides for Musca domestica, 2 strains: 2110

(a) Auburn (DDT-R) strain, 14 times as resistant to DDT as the Orlando DDT-susceptible strain. Tested by topical application of insecticides in acetone solution to adult insects:

Insecticide	Auburn Strain			Orlando Strain		
	LD_{50} (µg/fly)	.95 Fiducial Limits	LD_{50} (µg/g)	LD_{50} (µg/fly)	.95 Fiducial Limits	LD_{50} (µg/g)
Chlordane	29.0	(12- 57)	2791.3	42.0	(42- 84)	3586.8
Heptachlor	13.0	(11- 17)	855.79	11.0	(8.75- 15)	955.68
Methoxychlor	2.33	(2.03-2.53)	135.18	1.93	(1.33-2.33)	127.49
Chlorthion	0.14	(0.10-0.20)	10.52	0.21	(0.19-0.25)	16.89
Diazinon	0.06	(0.05-0.07)	3.01	0.10	(0.09-0.11)	6.15
American Cyanamid 4124	0.03	(0.03-0.03)	2.75	0.02	(0.02-0.03)	1.73

No significant difference in susceptibilities between the 2 strains except in case of Diazinon. Note overlapping of the fiducial limits.

(5) Toxicity of vapors of chlordane, others, to resistant and non-resistant strains, Musca domestica: 3320

(a) Strains: Orlando #1 exposed to DDT only: High DDT resistance, some cross resistance for lindane, dieldrin, chlordane; LDD: "Population" of dairy flies not controllable by DDT, dieldrin, lindane; resistance maintained by constant exposure of adults to residues on cages; Ballard: A wild strain from a dairy treated by space and residual lindane with poor control:

Insecticide	Lethal Time $_{50}$ (minutes)							
	Non-R		Orlando #1		LDD		Ballard	
	Vapor	Residue	Vapor	Residue	Vapor	Residue	Vapor	Residue
Chlordane	33	—	69	—	347	—	380	—
Lindane	25	10.9	58	16.4	173	65.6	316	229.3
Dieldrin	40	< 1	110	9.1	550	>120	550	—
Aldrin	< 15	—	23	—	158	—	96	—
DDT	—	9.0	—	ca1440	—	>240	—	343.4

(6) Toxicity of chlordane, and others, for Cirphis unipuncta (larva): 3268

Compound	Topical Application		Oral (Treated Leaves)		Ratio LD_{50} : LD_{99}	
	LD_{50} μg/g	Ratio to Parathion	LD_{50}μg/g	Ratio to Parathion	Topical	Oral
Chlordane	117.5	31.6	78.2	31.3	4.9	4.7
Parathion	3.7	1.0	2.5	1.0	3.4	8.5
DDT	193	52.2	45.7	18.3	4.7	22.8
Toxaphene	56.2	15.2	34.1	13.6	4.7	2.9
Lindane	28.1	7.6	27.9	11.2	3.2	5.1
Aldrin	19.8	5.4	11.4	4.6	3.7	24.7
Dilan	8.8	2.4	11.5	4.6	5.4	5.0
Dieldrin	8.3	2.2	4.6	1.8	3.1	3.8

(a) Parathion yielded fastest kill followed in order by Dilan, lindane, DDT.

(7) Toxicity of chlordane, and others, for Locusta migratoria migratorioides (young, virgin adults) by topical application; insecticides dissolved in tractor vaporising oil + cyclohexanone 90 to 10: 1585

Compound	LD_{50} 96 hrs		LD_{95}	
	μg/locust	μg/g	μg/locust	μg/g
Chlordane	20.4 ± 1.05	19.3	110.0 ± 30.9	104.0
Methyl parathion	0.94 ± 0.1	0.89	2.3 ± 0.52	2.2
Lindane	3.89 ± .21	3.69	12.9 ± 2.09	12.2
DNOC	10.4 ± .1	9.9	19.3 ± .897	18.3
Toxaphene*	40.2 ± 2.88	38.1	123.0 ± 16.9	116.0
DDT*	140.0 ± 7.6	133.0	258.0 ± 18.6	245.0

*LD_{50} 5 days

(a) Action of DNOC is most rapid, yielding paralysis within 30 minutes, and showing a mortality curve of steep slope; although lindane at LD_{50} is ca 3 times as toxic as DNOC, the two at probit 7.81 (99.75% kill) are equitoxic at ca 33μg/locust.

7) Pharmacological, pharmacodynamic, physiological, biochemical: Insects:

(I) Mode of entry:

a) Chlordane enters the insect body by way of the cuticle, by mouth and via the spiracular openings. Entry is influenced by state of the insecticide, for example, solution, dust, suspension, emulsion. Solutions in oil show enhanced toxicity over dusts and suspensions for many insects not susceptible to the latter. 353

(1) Tests with Musca domestica do not indicate any particular point of cuticular entry to be more vulnerable than others. 1561

(2) Toxicity for Musca of residual deposits of chlordane is enhanced by increasing temperature, for example, 70°F vs. 90°F. (positive temperature coefficient). 1561

(3) Chlordane is extremely effective for heavily sclerotized insects, for example, locusts, grasshoppers, roaches, ants. 353

(II) Physiological, Pharmacological

a) The action of chlordane is, on the surface, DDT-like, but it is not thought of as specifically neurotoxic. 2231, 2681

(1) The neurotoxic symptoms follow upon a distinct latent period. From 30 minutes—6 hours pass, during which the insect is passive, before there is marked increase in O_2 consumption. 353

b) In Periplaneta, the effect is depressant, with decreased muscle tone, and, (unless dosage is not too high) with weak but still coordinated movements. 353 2231, 520

(1) Elevated dosages may immobilize the subject at once, but the passive insect responds to stimulus with exaggerated movements, violent tremors.

(2) Has pronounced effect upon the action potentials of the crural nerve. After the latent period (3 hrs for α-chlordane, 8 hrs for β-chlordane, 5 hrs for technical chlordane) trains of high frequency discharges were registered from the crural nerve.

c) Honeybees, on contact with chlordane dusts, became highly agitated, and in four hours showed increasing loss of coordinated movement, with death following within 8 hrs. 909

d) Injection of chlordane to Blattella germanica was followed by a 4-8 hrs latent period, then followed by sudden rise in O_2 consumption to 5 times the normal level. 1441

e) On the motor nerves of isolated legs of Periplaneta americana and Calliphora erythrocephala chlordane exerts no stimulating effect. Apparently, action is at the ganglion and requires an intact reflex arc for manifestation. 295

(1) Distribution has been attributed to the haemolymph primarily, with the nerves secondarily taking part. Excretion of chlordane is via the Malpighian tubules.

f) The onset of the period of hyperactivity is correlated with the sudden rise in O_2 consumption in chlordane-injected Blattella germanica. 1441

g) Following chlordane injection, the heart of Periplaneta americana shows irregularity of pulsation both in intact and beheaded insects. The heart is arrested in diastole.

8) Action on beneficial insects:

a) Chlordane is hazardous to bees, which die in the field, away from the hive. 3099

(1) Highly toxic by oral, contact, or fumigant action. 909, 910

(2) As dusts on blooming alfalfa, chlordane has reduced the bee field force by 50-80%. Others report 25% kill in dusted blooming alfalfa (5% chlordane dusts). 910, 3098

b) Comparative toxicity of chlordane, and others, toward Apis mellifera by various routes of application and exposure: 1718

Compound	Oral Dose µg/bee to Yield % Mortality Indicated in 24 hrs.			Contact Spray Dose µg/cm² to Yield % Mortality Indicated			Effects of 1 Hour Contact With Residual Dry Films				Effects of Vapors from Residual Dry Films; Exposures of 1 Hour	
	20	50	90	20	50	90	% kill 24 hrs.	µg/cm²	Average Field Dose mg/cm²	Ounces Per Acre	% Kill 24 hrs.	µg/cm²
Parathion	0.018	0.04	0.144	0.144	0.257	0.354	90	0.54	0.0014	2	100	5.0
							10	.18			0	2.8
TEPP	.052	.065	.093	.358	.445	.621	8	.22	.0056	8	0	5.5
Lindane	.026	.079	.346	.772	.851	.986	100	.28	.0028	4	100	.44
							0	.074			0	.28
Dieldrin	.223	.269	.354	.386	.572	1.052	90	.09	.0014	2	100	.28
							10	.04			0	.074
Aldrin	.181	.239	.365	.327	.562	1.274	75	.09	.0014	2	100	.74
							0	.04			0	.074
Chlordane	.831	1.122	1.730	3.802	5.000	7.580	100	3.4	.0012	16	100	3.7
							12	.9			0	.37
Systox®	1.256	1.478	1.884	4.321	5.123	6.619	50	10.0	—	—	0	18.5
							22	6.8				
Dimefox®	1.25	1.905	3.506	16.52	23.17	38.64	0	50.0	—	—	0	74.0
Toxaphene	25.12	39.81	80.17	36.73	44.67	59.98	9	110.0	.0168	24	0	70.0
							0	40.2				

9) Chlordane in economic, practical insect control; field experiences:

1) considered superior to DDT in control of cucurlionids, cutworms, cercopids, agromyzid leaf-miners, Orthoptera, large Hemiptera. The residual action, due to volatility, is less than that of toxaphene, DDT. 353
2) For Melanoplus mexicanus, twice as toxic (contact) as DNOC, with high stomach, residual, toxicity. 359
3) Less effective as dust than BHC for Melanoplus spp. (Illinois), superior in Colorado. 3264, 2028
4) Chortoicetes (Australia), superior to BHC in control of. 43
5) For grasshoppers recommended at 1 lb/acre as spray, 1.5 lbs/acre as dust, 0.75 lb/acre as wettable powder (0.5 lb/acre for young nymphs). Less toxic than parathion for grasshoppers. Acts chiefly as a stomach poison, killing slowly. 1373, 2446, 2555, 1100, 334, 3267
6) Vs. Melanoplus mexicanus: 100% control with 4% baits at 15 lbs/acre. 354
7) Vs. Melanoplus spp: 0.5% in bran and oil baits at 5 lbs/acre, wet baits 0.5% chlordane at 20 lbs/acre, as effective as 6% sodium silicofluoride. 2446
8) Scapteriscus ucletus, S. vicinus controlled by 0.02% sprays at 100 gal./acre, 2% baits at 50 lbs/acre. 1769
9) Vs. Chlorocroa uhleri: Moderately toxic for. 353
10) Vs. Euschistus tristigmus: Effective for. 3368
11) Vs. Anasa tristis: More toxic than DDT for. 3222
12) Vs. Blissus spp: In turf, more toxic than DDT for. 2779
13) Vs. Lygus oblineatus, on alfalfa: <toxic than DDT for, relatively ineffective on peaches. 3327, 515, 2112
14) Psallus seriatus: Controlled by 2% dusts. 2438
15) Philaenus leucophthalmus: Complete control with 0.1% spray, superior to DDT, BHC. 511
16) Aphrophora spp, on alfalfa: Superior to DDT for. 3327
17) Psylla pyricolla: Completely ineffective for. 1359
18) Aphis persicae-niger: Ineffective for as a dust. 1733
19) Macrosiphum pisi: Inferior to DDT in the field for. 3016
20) Pseudococcus maritimus: 33-50% control, inferior to parathion, thiocyanates. 2356
21) Heliothrips hemorrhoidalis: Less toxic for than lindane, DDT. 2227
22) Taeniothrips simplex, T. inconsequens: As sprays, highly effective for. 2871
23) Thrips tabaci: Highly effective for. 3016
24) Pieris rapae: Inferior to BHC for. 3016
25) Estigmene acraea: Ineffective for, as dusts. 91
26) Anticarsia gemmatilis: Less toxic for than DDT, BHC, Toxaphene, Parathion, Methoxychlor, cryolite. 110
27) Laphygma: As a bait superior to other controls. 349
28) Cirphis, Prodenia: As sprays, = to DDT; as dusts, inferior to DDT. 3016, 300
29) Laphygma frugiperda: Controlled by 10% dusts. 91
30) Agrotis orthogonia: Effective against. 350
31) Heliothis armigera: As dusts inferior by far to DDT, cryolite. 1033

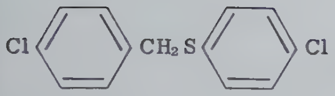
32) *Argyrotaenia velutinana*: Valueless against. 1199
33) *Carpocapsa pomonella*: Ineffective against. 3263
34) *Pyrausta nubilalis*: Inferior to DDT in control by aircraft sprays. 353
35) *Diatraea saccharalis*: Poor control with. 1649, 1650
36) *Melittia satyriniformis*: Ineffective against. 1614
37) *Profenusia canadensis*: Inferior to BHC against. 1360
38) *Cephus cincta*: Resistant to sprays of. 353
39) *Hylemyia brassicae*, *H. floralis*: $>$ toxic than DDT as emulsion on seedlings. 3016
40) *Hylemyia brassicae*, *H. floralis*, *H. cilicrura*, *H. trichodactyla*, on rutabagas: Inadequate, even at high rates in control of, in British Columbia. 1800
41) *Hylemyia cilicrura*: Soil treatment with controls. 1034
42) *Anastrepha ludens*: Inferior to DDT in control of. 42
43) *Dacus dorsalis*: 5 times as effective as DDT, but inferior to aldrin, dieldrin. 483
44) *Liriomyza orbona*, *L. pusilla*, *L. flaveola*: Very effective against, dusts yielded 99% control. 1691
50) *Epilachna varivestis*: Relatively ineffective against; = to DDT. 3016
51) *Ludius aeripennis*: $<$ effective than lindane, requiring 4 times the lindane dosage for = effect. 2583
52) *Horistonotus uhlerii*: Controlled by, in cotton fields. 91
53) *Melonotus*, *Conoderus*: Controlled by 1% dust at 400 lbs/acre; ineffective as seed pretreatment. 435
54) *Popillia japonica*: Highly effective for as a soil treatment, 10 lbs/acre yielded 99.6% + kill. 1022, 2777, 2778
55) *Lepidoderma* spp: Of no value against. 353
56) *Leptinotarsa decemlineata*: = or $<$ effective than DDT. 3016, 1872
57) *Epitrix cucumeris*: More effective than calcium arsenate for. 1872, 3143
58) *Epitrix hirtipennis*: Sprays yielded 90-95% control of. 820
59) *Diabrotica duodecempunctata*: As soil dust 4 lbs/acre very effective; against adults sprays $<$ effective than BHC yielding 50% as against 75% control. 1876, 811
60) *Hylobius radicis*: $<$ effective for than BHC. 2813
61) *Hypera postica*: Much superior to DDT in control of. 1447
62) *Brachyrhinus ligustici*: Much superior to toxaphene for. 1312
63) *Anthonomus grandis*: Toxic to larvae, which die on emergence. 2578
64) *Anthonomus signatus*: Inferior to DDT, cryolite, for. 2143
65) *Conotrachelus nenuphar*: Highly effective against, as 0.1% spray 4 times repeated; most effective also vs. adults. 1606, 516
66) *Acarina*: Poor plant acaricide. 2373
67) *Eutrombicula alfreddugesi*: Excellent control of at 2 lbs/acre; also *Acariscus mansoni*. 2863
68) *Amblyomma americana*: As area spray at 2 lbs/acre disinfestation lasting ca 2 months.
69) *Periplaneta americana*, *Blattella germanica*, *Blatta orientalis*: 100 mg/ft^2, residual, gave high control for 8 weeks; LD acquired in 10-20 minutes of contact. 1094, 1371
70) *Monomorium pharaonis*: Most effective control at 2% solution, emulsion, dust. 3287
71) *Iridomyrmex humilis*: 2% dusts, emulsions yielded complete control. 3287
72) *Camponotus pennsylvanicus*: 2% solutions, emulsions controlled. 1637
73) *Pogonomyrmex barbatus*: 3% solutions gave control. 334
74) *Solenopsis saevissima*: 5% formulations superior to DDT, BHC, toxaphene. 2060
75) *Lasius americanus*: 0.3% suspension sprays on turf yielded 90% control. 1780
76) *Haematoptinus adventicius*: 0.2% emulsions yielded complete control of. 3026
77) *Bovicola bovis*, *Solenoptes capillatus*, *Linognathus vituli*, *Haemoptinus eurysternus*: 3 seasons tests on dairy herds showed 0.25% chlordane, alone, (others DDT, BHC, rotenone-sulfur) giving excellent seasonal control with 1 application. 1904
78) *Anopheles quadrimaculatus*, *Aëdes aegypti*: Order residual effectiveness: DDT $>$ BHC, chlordane $>$ toxaphene; 200 mg/ft^2 chlordane yielded complete kill for 4 weeks. 1094
79) *Simulium* spp: Effective against, but $<$ so than DDT. 1192
80) *Musca domestica*: As space and direct contact spray superior to DDT; residual effectiveness DDT $>$ BHC $>$ chlordane $>$ toxaphene $>$ DDD. Most effective on DDT-R strains. Highly toxic (LC_{50} 23 ppm) vs. maggots when combined with medium. 1094, 971, 2466, 1172, 351
81) *Siphona irritans*: Very effective against. 914, 1884, 2861
82) *Melophagus ovinus*: 0.2% suspension dip or spray superior to DDT, DDD but inferior to rotenone. 959
83) *Attagenus piceus*: 0.5% on clothing was more toxic than DDT but not as long lasting. 1926
84) *Latrodectes mactans*: Effective against, but $<$ so than DDT.

For extensive screening data consult Reference 1801.

31

p-CHLOROBENZYL-p-CHLOROPHENYL SULFIDE

(p-Chlorophenyl-p-chlorobenzyl sulfide; Chlorbenside; Chlorocide; Chloroparicide; Chlorparacide; p,p′-Dichlorodiphenyl sulfide.)



Molecular weight: 269.19

GENERAL

635, 1524

An acaricide of recent introduction (1953). Very toxic to the eggs and larvae of tetranychid mites, with activity, to some extent, against the adult stage. Highly toxic for the winter and summer eggs, and young of *Metatetranychus ulmi* (=*Paratetranychus pilosus*), and the eggs and young stages of *Tetranychus telarius*. Specifically acaricidal, without activity against the eggs, larvae or adults of any insect tested. Predatory insects, for example *Blepharidopterus angulatus*, adult and larval Coccinellids, Syrphids, Anthocorids, the predatory mite *Typhlodromus* in sprayed orchards have not, in preliminary observations, been found affected.

Residues are persistently ovicidal for mite eggs and, at sub-ovicidal levels, have stomach toxicity for mite larvae. Adult mites are largely unaffected and, normally, there is a lapse of 2-3 weeks before an active infestation is controlled. Non-systemic in action, but capable of penetrating and diffusing across leaves from one surface to the other although mite control by this property demands high dosages.

PHYSICAL, CHEMICAL

White, crystalline solid; m.p. 72.5°C; v.p. 6.1×10^{-5} mm Hg at 40°C; practically insoluble in water; low solubility in alcohols, petroleum oils; soluble in acetone, aromatic hydrocarbons; the following solubilities in g/100g solvent are noted: at 20°C acetone 92g, benzene 111g, toluene 107g, xylene 93g, methanol 4g, ethanol 2.8g, carbon tetrachloride 49g, chloroform 99g, dioxane 102g, acetic acid 63g, methyl ethyl ketone 137g, odorless kerosene 5-7.5g; stable to reduction, acid, and alkaline, hydrolysis; readily oxidized to the sulfoxide, and more slowly to the sulfone (non-volatile) via the sulfoxide; the resulting sulfoxide, sulfone, have acaricidal properties; for *Paratetranychus citri* adults, the related phenyl benzyl ethers are effective acaricides; highly lipoid soluble; possesses an appreciable vapor pressure. Formulated as wettable powders, emulsifiable concentrates. Compatible with practically all other pest control substances. 2231, 1953 635

TOXICOLOGICAL

1) Of low toxicity for mammals. Oral doses, 250 mg/k /day, during 3 weeks, did not affect growth, haematological findings in rats: Livers moderately enlarged without pathology. A daily dose of 50 mg/k/day produced no observable effects when given over 3 weeks. 2231 1953

2) Mouse or LD_{50} = > 3000 mg/k. 2231

3) Phytotoxicity:
   - a) A selective phytotoxicity for some cucurbits has been noted. 635
   - b) No phytotoxicity shown for apples, pears, plums, peaches, grapes, soft fruits, glasshouse crops, ornamental plants. 635

4) Toxicity for and uses in control of acarines and other arthropods:
   - a) Sprays of miscible oil solutions, or dispersible powders, at 0.05%, applied at the green cluster to pink bud stage on apples (white bud on pears) have given outstanding control of *Metatetranychus ulmi*. Best results are given by application as late as possible before blooming, before the main hatching of winter eggs, to obtain optimum ovicidal and larvicidal effects with maximum of retentive leaf area to hold the deposits. In favorable circumstances, such application gives season long red spider control. As a miscible oil spray, effective at bud burst, but without persistent foliage deposit. 635
   - b) As ovicide, for summer mite eggs, 2 applications at 3-4 week intervals beginning (England) at mid-June; 0.02% dispersible powders, 0.0125% miscible oil solutions, give good control. 635
   - c) Gives control of *Tetranychus telarius* on soft fruits and herbaceous plants in the greenhouse and outdoors, but best use is as a protective, to prevent build-up of active infestation, rather than as an eradicant. 635
   - d) A reason given for the persistent effect on foliage is the acaricidal activity of the sulfoxide and the sulfone to which p-chlorobenzyl-p-chlorophenyl sulfide is slowly converted under field conditions. 1953
   - e) Reported to be a highly effective stomach poison for *Tinea*. 1933
   - f) Reported to be highly larvicidal to *Anopheles*. 767
   - g) Poor contact insecticide for *Epilachna*, *Oncopeltus*, *Musca*. 1595, 3033

32

CHLOROBROMOPROPENE (1-Chloro-3-bromopropene-1)

$CHCl = CH_2 - CH_2Br$ Molecular weight: 214

GENERAL

An insecticidal fumigant, suitable for the fumigation of fresh, perishable fruits. 255

PHYSICAL, CHEMICAL

A liquid; $d_{4°}^{20°}$ 1.40; v.p. 40 mm Hg$^{25°C}$; flash point > 90°F; soluble in water to 0.2 g/100 cc. 3199

TOXICOLOGICAL

1) Toxicity for higher animals: 3199

Animal	Route	Dose	Dosage	Remarks
Mouse	Intragastric	LD_{50}	0.1 ± 0.008 g/k	Suspension in propyleneglycol.
Rat	Intragastric	LD_{50}	0.078 ± 0.008 g/k	Suspension in propyleneglycol.
Mouse, Rat	Inhalation	LC_{50} (10 hrs)	260 ± 50 ppm	Exposure 4 hours.
Rabbit	ct	LD_{50}	2.0 ± 0.3 g/k	Via unabraded, shaved skin.

a) Intragastric administration yielded hyper-excitability, followed by tremors, failure of coordination, depression, dyspnoea.

b) Dead subjects showed: Fluid and gas distension of stomach, erosion (sometimes with hemorrhage) of gastro-intestinal mucosa; sometimes observed are fatty degeneration of liver and lung hemorrhage.

c) Inhalation yielded symptoms as above, plus great respiratory distress, with dyspnoea, hyperpnoea, mucous nasal discharge, lacrimation. Dead subjects showed severe oedema of lungs.

d) Repeated exposures; chronic toxicity:

(1) Repeated exposure (inhalation), for 0.5, 1, 4, 8 hours to 50-1900 ppm, yielded varying degrees of nose and eye irritation, and respiratory distress (even at 50 ppm), and moderate CNS depression, with prolonged exposure at higher concentrations.

(2) Chronic exposure (rat, mouse) at 1 hour daily exposures, 5 days/week, 60-20 exposure periods, to 100-563 ppm showed slight irritation of nose, eyes, and slight respiratory depression during exposure. At 100 ppm: No toxic effects. At 150, 225 ppm: Moderate growth retardation with greater eye, nose, respiratory, irritation. All ♂ animals dead after 11 exposures to 375 ppm; ♀ animals all dead after 15 exposures. Mice somewhat > tolerant than rats. Gross lesions of respiratory tree, fluid accumulation in thorax, distension of gastro-intestinal tract were exhibited at autopsy.

(3) 0.5 cc applied cutaneously to shaved rabbits, as propylene glycol suspension, yielded severe irritation of skin; 0.01 cc of a 5-40% suspension, in eye, yields irritation in rabbit comparable to allyl alcohol, diethanolamine, Tincture of Green Soap (U.S.P.)

e) In man:

(1) Concentrations as low as 0.1 ppm may yield mild irritation in some; 2 ppm cause mild irritation in 2 minutes, moderate irritation in 3 minutes, severe irritation in 4 minutes. 50 ppm yield immediate, mild irritation, and in 0.4 minutes severe irritation.

(2) Comparison of toxicity of chlorobromopropene and other fumigants, for naked 23-26 hour old eggs and 3rd instar larvae, of Dacus dorsalis, (Oriental fruit fly): 255

(a) Exposure 2 hrs at 71-80°F as tested in empty vessel fumigation:

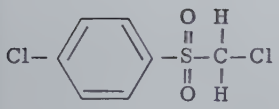
Fumigant	Eggs		Larvae	
	LD_{50} (mg/l)	LD_{95} (mg/l)	LD_{50} (mg/l)	LD_{95} (mg/l)
Chlorobromopropene	5.9	8.7	2.0	3.1
Acetonitrile	44	75	> 82.4	—
Chloroacetonitrile	1.2	1.5	< 1.3	< 1.3
Acrylonitrile	1.2	1.6	< 1.2	1.6
Acrylonitrile + CCl_4 50:50	3.7	11	1.7	4.9
Carbon disulfide	53	92	56	89
Carbon tetrachloride	> 167.8	—	> 167.8	—
Methyl iodide	< 2.9	< 2.9	< 2.9	4.2
Methyl thiocyanate	2.7	8.5	< 1.4	< 1.4
1-Bromo-2-chloroethane	< 2.2	< 2.2	< 2.2	2.3
Ethylene dibromide	< 2.9	< 2.9	< 2.9	< 2.9
1, 3-Dichloropropene	3.9	8.7	6.0	13.5
Ethyl chloroacetate	6.2	13.5	1.4	3.6
Methyl bromide	15.0	24.5	9.2	18.5

Fumigant	Eggs LD_{50} (mg/l)	Eggs LD_{95} (mg/l)	Larvae LD_{50} (mg/l)	Larvae LD_{95} (mg/l)
Methyl formate	65.0	110.0	—	—
Hydrogen cyanide	10.0	26.0	1.3	2.8
Propylene oxide	> 89.4	—	18.5	28.0
Ethylene oxide	6.2	12.0	8.7	17.0
Ethylene dichloride	2.3	5.9	38	120.0
Ethyl formate	> 104	—	—	—
1, 1, 1-Trichloroethane	28	69	< 139	—
sym-Tetrachloroethane	25	68	20	43
1, 1-Dichloro-1-nitroethane	24	60	< 1.9	< 1.9
Allyl chloride	71	105	70	> 98.6
Allyl bromide	15	24	1.8	7.5

33

CHLOROMETHYL-p-CHLOROPHENYL SULFONE

(Lauseto Neu; p-Chlorophenyl chloromethyl sulfone; Chloromethyl-4-chlorophenyl sulfone.)



GENERAL

[Refs.: 1059, 418, 414, 2231, 919, 1810, 2566]

A German insecticide brought forward as Lauseto Neu, a particularly powerful and effective ovicide for human body lice, e.g. *Pediculus humanus corporis*. Very effective against adult lice and bed bugs, but of little value against flies and aphids. Has proven to be ovicidal to *Metatetranychus ulmi*. Compared with certain others, Lauseto Neu has proved to be the outstanding ovicide for human lice, as follows: Lauseto Neu > 2, 4-dinitrophenyl propionate, 2-benzylpyridine, 3, 4-dichlorobenzyl cyanide, diallyl adipate, diallyl succinate, diazoaminobenzene. Has been reported as effective vs. the larvae of *Pyrausta nubilalis*.

PHYSICAL, CHEMICAL

1) A solid; m.p. 122°C; soluble in petroleum oils and various organic solvents.

TOXICOLOGICAL

1) *Toxicity for higher animals*: No data available to this compilation.

2) *Toxicity for insects*:

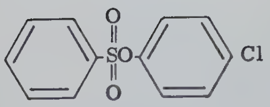
a) Comparative toxicity of Lauseto Neu and other compounds for *Cimex lectularius*, and *Pediculus humanus corporis*, as contact sprays in white (P31)oil, the solutions applied at the rate of 0.36 mg spray/cm^2 : 414

Insecticide	LC_{50} (% Concentration) At Deposit of 0.36 mg/cm^2 *Cimex lectularius*	LC_{50} (% Concentration) At Deposit of 0.36 mg/cm^2 *Pediculus humanus corporis*
Lauseto Neu	0.2	0.1
Lindane	.05	.02
DDT	.5	.3
Methoxychlor	.5	.9
DDD	1.2	.9
DFDT	5.0	1.4
Lethane ® 384	—	1.5
Lauryl thiocyanate	—	5.0
Lethane ® 60	—	8.1

b) Vs. *Pyrausta nubilalis* (larva) at 1 lb per 100 gallons spray yielded 100% control without plant injury. 2566

34

p-CHLOROPHENYL BENZENE SULFONATE
(4-Chlorophenyl benzene sulfonate; PCBS;
PCPBS; PCl; Murvesco.)



Molecular weight: 284.707

GENERAL

[Refs.: 1953, 2231, 1774, 1810, 2589, 1513, 1511, 353]

An acaricide, closely related to Ovotran ® (p-chlorophenyl-p-chlorobenzene sulfonate) q.v., recently (1952) brought forward as an experimental acaricide. Some tests have indicated an ovicidal action (vs. Tetranychus bimaculatus) inferior to that of Ovotran®; other experimenters have gotten results vs. Tetranychus telarius, Metatetranychus ulmi showing equal, or greater ovicidal action when compared with Ovotran®. Marked toxicity to summer eggs of Metatetranychus ulmi. More toxic than lead arsenate for Carpocapsa pomonella (codling moth).

PHYSICAL, CHEMICAL

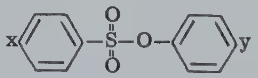
Pure, a colorless crystalline solid, commercial product: Off-white to pink; m.p. 61-62°C (pure) 56-69°C (commercial); virtually insoluble in H_2O; soluble in polar and aromatic organic solvents; hydrolyzes in presence of alkali to phenol and alkali sulfonate; compatible with commonly used spray materials. Formulated as greenhouse aerosols, 20% wettable powders, miscible concentrates (used at 0.025-0.05% active).

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) No data available; by analogy with Ovotran ® probably not highly toxic.

2) Phytotoxicity:
   a) Not to be applied to Cucurbitaceae or to young tomatoes in the greenhouse; suspected of fruit damage 1953, 353
   in apple orchards. Not phytotoxic for many apple varieties, pear, plum, damson, peach, black currant, 1511
   hop varieties nor, under glass, to carnations, older tomatoes. The damage to cucurbits takes the form of shoot hardening. The damage to some varieties of apple (England) occurs under hot, dry conditions and strong sunlight, with symptoms of damage slow to develop.

3) Toxicity for acarines, insects:
   a) Toxicity of p-chlorophenyl benzene sulfonate for Tetranychus bimaculatus and Epilachna varivestis (3rd 1774
   instar) compared with certain other substituted phenyl benzene sulfonates:



(** = p-chlorophenyl benzene sulfonate.)

Ring Substitution		Minimum LD_{100} (lbs/100 gal) For		
at X	at Y	Tetranychus bimaculatus		Epilachna varivestis (3rd instar)
		Adult	Egg	
unsubstituted	unsubstituted	> 3.0	> 3.0	> 3.0
** "	4-chloro	3.0	3.0	3.0
4-chloro	unsubstituted	> 3.0	3.0	3.0
4-chloro	4-chloro (Ovotran ®)	> 3.0	0.06	0.5
4-chloro	2,4-di-chloro	> 3.0	> 3.0	> 3.0
4-chloro	2,4,5-tri-chloro	> 3.0	> 3.0	> 3.0
4-chloro	2,4,6-tri-chloro	> 3.0	> 3.0	> 3.0
4-chloro	tetrachloro	> 3.0	> 3.0	> 3.0
4-chloro	pentachloro	> 3.0	> 3.0	3.0
4-chloro	4-bromo	> 3.0	0.25	1.0
4-chloro	4-methyl	> 3.0	> 3.0	> 3.0
4-chloro	2-sec-butyl	> 3.0	3.0	3.0
4-chloro	4-tert-butyl	> 3.0	> 3.0	> 3.0
4-chloro	2-allyl	> 1.0	> 1.0	> 1.0
4-chloro	4-methallyl	> 3.0	> 3.0	3.0
4-chloro	4-methoxy	> 3.0	> 3.0	1.0
4-chloro	4-nitro	> 3.0	> 3.0	> 3.0
4-chloro	2-cyclohexyl-4,6-dinitro	> 1.0	> 1.0	> 1.0
4-chloro	2-phenyl	3.0	> 3.0	> 3.0
4-bromo	4-chloro	> 3.0	0.5	2.0
4-bromo	4-bromo	> 3.0	> 0.5	> 3.0
3-nitro	4-chloro	> 3.0	> 3.0	> 3.0

b) Applied directly, as 5% spray or dust, to Periplaneta americana, no deaths occurred among the treated insects which were freed of mites, with restoration of full vigor to the colony. 1011

c) Liponyssus bacoti (tropical rat mite), controlled on white mice by 10% dusts, applied in twice weekly treatments in less than 1 month. No toxic symptoms observed in the mice. 1011

d) Field experiments with p-chlorophenyl benzene sulfonate to control Metatetranychus ulmi on apple trees: 1511

(1) Applied as a 20% wettable powder at 2 1/2 lbs/100 gal (U.K.) (1/2 lb active ingredient) + 8 fluid oz 20% miscible parathion: Egg count at start / 180 leaves = 3911, mite count at start / 180 leaves = 4946; 10 days after spraying eggs / 180 leaves = 2957, mites / 180 leaves = 11; 20 days after treatment eggs / 180 leaves = 31, mites / 180 leaves = 17. By contrast trees sprayed with diphenyl sulfone at 1 lb/100 gal (U.K.) with parathion 8 fluid oz 20% miscible with egg, mite count / 180 leaves at start of 1801, 1841 showed, in 10 days after treatment, eggs, mites/180 leaves = 1955, 129, and 20 days after treatment eggs, mites / 180 leaves = 3073, 4597. Treatments in June.

(2) Two treatments of 20% wettable powder at 2.5 lbs/100 gal (U.K.): Initial count / 180 leaves eggs = 215, mites = 86, in the experimental, and 114, 70 in the control, plot with treatments 16 days apart; 9 days after final treatment eggs / 180 leaves = 0, mites / 180 leaves = 0 (experimental plot) eggs, mites / 180 leaves = 961, 560 (control plot).

(3) 20% wettable powder at 3 3/4, 2 1/2, 1 1/4 lbs (3/4, 1/2, 1/4 lbs actual active ingredient) in two applications at 10-14 days interval gave practically 100% control of Metatetranychus ulmi. Results were equally good with one application supplemented by parathion at 0.01%, rotenone at 0.004%. Wettable powders slightly > effective than miscible concentrates. Not effective against winter eggs of M. ulmi.

e) Greenhouse experiences with p-chlorophenyl benzene sulfonate as an aerosol at $5 g/1000 ft^3$ and as a thermal smoke to control Tetranychus telarius: 1511

(1) High degree of control obtained.

(2) Eggs were efficiently killed when PCBS was on upper, and eggs on underside, of leaves. Marked contrast to action of diphenyl sulfone.

(3) Residual effect of sprayed surfaces, after use of wet sprays, continued for 4-6 weeks.

(4) Prevented egg hatching, killed newly hatched mites. Not highly effective against adults, but the eggs laid by these were either prevented from hatching, or, if hatched, the young were killed.

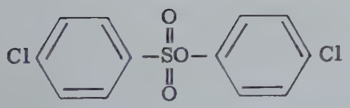
(5) Slow acting; one month required for full effect.

f) Recommended use: 1/4 lb/100 gal (U.K.) with parathion 0.01%, or rotenone 0.004%.

35

p-CHLOROPHENYL-p-CHLOROBENZENE SULFONATE

(4-Chlorophenyl-4-chlorobenzene sulfonate; Ovotran®; K-6451.)



Molecular weight: 303.16

GENERAL

[Refs.: 118, 117, 191, 1698, 1812, 1811, 2851, 2867]

An acaricide highly toxic for eggs and immature stages of phytophagous mites, but comparatively ineffective, and with little "knockdown" potential, for adult stages. Possesses an effective residual ovicidal action, and some contact toxicity through the leaf surface, killing on the side of, or face of, the leaf opposite to that on which it is deposited. No systemic action is present. Used as an aerosol, controls the hatching young of the acaricide resistant strain of red spider mites, when used at dosages decidedly higher than those needed for non-resistants. The residual toxicity mentioned above is marked for eggs and newly hatched mites, but is low for adults. These survive in great number to deposit eggs which, however, generally are killed before hatching, or the newly-hatched immature mites are killed on the residues. Additions of parathion, at 8 oz per acre, to Ovotran® permits high initial kills of Paratetranychus citri, as do additions of bis-(p-chlorophenoxy)-methane, Aramite®, TEPP, tetraethyl dithiophosphate (ASP-47). These additions, however, do not extend the residual control, nor result, on citrus, in significantly more effective ultimate control. See the section titled Miticides of Acaricides.

PHYSICAL, CHEMICAL

Crystalline, colorless or white to tan, flaky, solid; m.p. 86.5°C; v.p. low; virtually insoluble in water; soluble in petroleum oils and many organic solvents for instance (as g/100 g solvent at 25°C) acetone: 130, carbon tetrachloride: 41, cyclohexanone 110, 95% ethanol: 1.4, ethylene dichloride: 110, Deobase oil: 2, Shell 8230 oil: 2.7, Velsicol AR-60: 52, xylene: 78; very stable, although hydrolyzed by alkalis; compatible with most spray materials. Formulated as 50% wettable powders, dusts, aerosols or miscible oil concentrates.

TOXICOLOGICAL

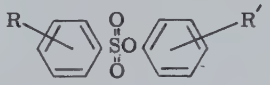
1) Acute toxicity, higher animals:

Animal	Route	Dose	Dosage (g/k)	
Rat	or	LD_{50}	2.05	836

2) Chronic toxicity, higher animals:
   - a) Rats, receiving in diet 300 ppm for 130 days, tolerated Ovotran ® without overt, or histologically demonstrable, ill effects; at 1000 ppm the beginnings of liver injury were noted. 836
   - b) Reported to have caused both liver and kidney damage in animals undergoing chronic toxicity tests. 129
   - c) May produce skin irritation in human subjects. 129
   - d) Generally, to be considered of low mammalian toxicity.

3) Phytotoxicity:
   - a) Has been used successfully without damage, under proper conditions, on cotton, deciduous fruits, nut trees, ornamentals. 129
   - b) "Russetting" of apples, pears, and damage to hops has been reported and injury to raspberries suspected. 129, 2867
   - c) Safe on roses only in the spring and summer; in seasons of shorter day length leaf drop was marked. 2867
     - (1) As spray, controls resistant red spider mites, but may produce injury, and induces leaf drop during shorter days.
   - d) On citrus trees, orange, lemon, at 4 lbs per 100 gallons and 1500 gals per acre, with temperatures for 10 successive days at 95°F or above, there occurred no injury to fruits or mature leaves of citrus; a slight pitting of the underside of young leaves of lemon was noted. 1698

4) Toxicity for acarines:
   - a) Ovicidal activity of substituted phenyl benzene sulfonates; structure and miticidal activity. [after Ref. 2231 quoting 1744, 1811, 2851.]



	R	R′	LC_{100} (lbs/100 gals) *Tetranychus bimaculatus*	LC_{50} (%) *Tetranychus telarius*
(Ovotran ®)	4-Cl	4-Cl	0.06	0.033
	H	H	> 3	.051
	H	4-Cl	3	.014
	4-Cl	H	3	.67
	H	2,4-di-Cl	—	.053
	4-Cl	2,4-di-Cl	> 3	.32
	2,4-di-Cl	4-Cl	—	> .5
	2,4-di-Cl	H	—	.3
	4-Cl	2,4,5-tri-Cl	> 3	—
	2,4-di-Cl	2,4-di-Cl	> 3	> 0.5
	4-Cl	2,3,4,6-tetra-Cl	> 3	—
	4-Cl	penta-Cl	> 3	—
	4-Cl	4-Br	0.25	—
	4-Br	4-Cl	.5	—
	4-Br	4-Br	> .5	—
	4-Cl	4-CH_3	> 3	—
	4-Cl	4-OCH_3	> 3	—
	4-Cl	4-NO_2	> 3	—
	3-NO_2	4-Cl	> 3	—
	4-Cl	$4\text{-C(CH}_3)_3$	> 3	—
	4-Cl	$2\text{-C}_6\text{H}_5$	> 3	—

   - b) LC_{50} (g/100 cc) of Ovotran ® for developmental stages of *Tetranychus bimaculatus*, placed on bean leaves treated in the settling tower (method of Ebeling and Pence): 905

Ovotran ® as	LC_{50} (g/100 cc) 2 Days Following Treatment			
	Adult	Larva	Egg	Adult (On Leaf Surface Opposite Treated Surface)
Emulsifiable concentrate	.45	.019	.076	> 5.0
Wettable powder	4.25	.028	.109	> 5.0

   - c) Toxicity of Ovotran ® for *Tetranychus bimaculatus*: 117
     - (1) Residual toxicity in greenhouse tests on *Phaseolus coccineus* (scarlet runner bean).

	lbs/100 gals		% Mortality At Days Between Spraying and Infesting Plants				
	Formulation	Active ingredient	1 day	3 days	7 days	10 days	14 days
50% powder	2.0	1.0	90.3	75.6	82.8	91.4	80.3

(2) Residual toxicity to Tetranychus bimaculatus, using 50% wettable powder at 2 lbs per 100 gallons, in greenhouse tests on Phaseolus coccineus; more than 1000 mites examined in every instance:

Days Between Spraying and Infesting Plants	% Mortality After		
	7 days	14 days	21 days
1	77.3	90.3	93.9
2	45.4	84.0	81.1
3	33.6	75.6	83.8
4	65.4	73.8	81.9
5	89.3	87.4	89.1
6	80.4	90.7	85.6
7	62.4	82.8	91.2
10	87.0	91.4	90.2
14	69.1	80.3	85.8
Control	5.6	3.4	2.9

(3) Residual ovicidal toxicity, Ovotran® as 50% wettable powder at 3 lbs per 100 gallons; greenhouse tests; 6 mature ♀ Tetranychus bimaculatus/plant remaining for 5-6 days:

Days Between Spraying and Infesting	Age of Residue On Which Eggs Laid	Days From Spraying To Examination	Total Eggs Laid	% Mortality Of Eggs
1	1-5	14	146	91.8
6	6-11	19	261	85.5
10	10-16	23	261	99.2
15	15-20	28	182	86.3
20	20-25	33	180	85.6
24	24-29	37	198	80.9
27	27-32	40	186	78.5
29	29-34	42	51	45.1
31	31-36	44	82	24.4
38	38-43	52	112	16.1
45	45-50	59	40	5.0
Control			172	7.0
"			138	5.1
"			156	23.7

(4) For comparison with (2), residual toxicity of 2,4-dichlorophenyl benzene sulfonate (Miticide 923), used as a 50% emulsifiable concentrate at 1 : 400 against Tetranychus bimaculatus on Phaseolus coccineus; ca 700 mites examined in each case:

Days Between Spray and Infesting Plants	% Mortality After	
	7 days	14 days
1	73.4	46.8
2	37.7	15.0
3	39.8	41.6
4	39.4	28.1
5	28.8	37.5
6	23.0	10.5
7	33.6	12.1
10	60.8	32.6
14	14.8	27.6
Control	3.4	2.6

Eggs produced by surviving mature females survived the residues in great number.

d) Tetranychus pacificus: Poor control using Ovotran® as wettable powder at 1.5 lbs/100 gal, although 1 lb/100 gals gave good control of Tetranychus bimaculatus, Metatetranychus ulmi, Eotetranychus carpini borealis, Bryobia praetiosa in apple orchards under Pacific Northwest conditions. 727

e) Aceria sheldoni: Poor to no control with Ovotran® as wettable powder, emulsifiable concentrate, on citrus trees. 1699

f) Paratetranychus pratensis: On wheat, less than 75% mortality using Ovotran®. 1442

g) Half-life of Ovotran® on citrus peel = 10 days 1302

h) Effect of Ovotran® as a spray at various dosages, at rate of 1600 gals/acre, in citrus orchards, for Paratetranychus citri; compared with medium petroleum oil. Average number of adult mites / 32 leaf sample: 1698

Orchard	Sprayed	Test Interval (days)	Ovotran ®		Petroleum Oil	
			Dosage/100 gal	Av No./Sample	Dosage/100 gal	Av No./Sample
I	May	88	5 oz	0.7	1.75 gal	0.4
II	July	73	8 oz	2.0	1.75 gal	4.0
III	October	304	16 oz	18.0	1.75 gal	25.0
			32 oz	5.0		

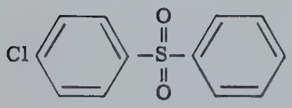
Compared with bis-(p-chlorophenoxy)-methane. Average number adults/32 leaf sample:

Orchard	Sprayed	Test Interval (Days)	Dosage (lbs/acre)	Ovotran® Av No/Sample	Bis-(p-chlorophenoxy)methane Av No/Sample
Lemon	October	304	16	14	43
Lemon	July	73	8	2	7
Orange	March	90	2	38	
			4	17	51
			8	12	
Lemon	July	91	5	0	12
			10	0	4
Orange	April	96	4	4	
			8	3	8
Orange	April	106	5	2	
			10	1	3
Orange	March	138	4	3	
			6	4	7
			8	2	4
			12	1	
Lemon	September	244	12	1	2
			16	0	153
Used as semi-concentrates at 200 gals/acre.					
Orange	May	15	4	1	48
Orange	May	25	4(+DDT 6 lbs/acre)	1	11
Orange	May	42	4	1	27
Orange	March	58	6	1	8
Orange	May	58	4(+DDT 6 lbs/acre)	1	11
Orange	April	62	4.8	0	21
Orange	March	64	3.0	1	4
Orange	May	92	3.6	6	6
Orange	October	304	6 (at 400/gal/acre)	2	74

36

p-CHLOROPHENYL PHENYL SULFONE

(4-Chlorodiphenyl sulfone; R-242; Sulfenone®; Sulphenone.)



Molecular weight: 253

GENERAL

[Refs.: 1933, 1953, 191, 1698, 1812, 900, 214, 129, 1801, 1459]

An acaricide of restricted insecticidal action which shows effective residual toxicity and ovicidal action for Tetranychus bimaculatus and other phytophagous mites. Also see the general treatment of Miticides or Acaricides in this work. Of little toxicity to honeybees and beneficial insects.

PHYSICAL, CHEMICAL

A white solid, or colorless crystals; m.p. 98°C, said to exist in 2 forms of m.p. 90°C and 94°C; virtually insoluble in water; slightly soluble in petroleum oils; readily soluble in polar and aromatic organic solvents; solubility (in g/100g solvent) acetone: 74.4, dioxane: 65.6; isopropanol: 2.1; n-hexane: 0.4; benzene: 44.4; toluene: 29.4; xylene: 18.2; carbon tetrachloride: 4.9; stable toward acids, alkalis, oxidants and reductants, at normal temperatures; compatible with commonly employed spray substances; tasteless; aromatic odor; the technical product contains small quantities of diphenyl sulfone and p,p′-dichlorodiphenyl sulfone. Formulated as 40-50% wettable powders, 25% emulsions, dusts; wettable powders used at 2-3 lbs/100 gallons.

TOXICOLOGICAL

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage (g/k)	Remarks	
Mouse (albino)	or	LD_{50}	2.7	Crude compound.	129, 1459
" "	ip	LD_{50}	1.0	" "	
Rat "	or	LD_{50}	> 1.4	" "	129, 1953, 1459
" "	ip	LD_{50}	ca 0.5	Pure compound.	
Mouse " ♂♂	or	LD_{50}	3.65	Toxicity for rats is of the same order.	3319
Rat	or	LD_{50}	> 2.0		1459

a) Mice, receiving in the diet 100 ppm for 12 months, showed no overt signs of intoxication. 129

b) Rats, receiving in the diet 1000 ppm for 2 months, showed no signs of intoxication. 3319

c) No evidences of chronic toxicity, or dermal irritation, in exposed rats. 1953

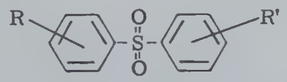
d) 10, 100, 1000 ppm in diet, rat, for >2 yrs yielded retardation in weight gain only at 1000 ppm. 1459
10, 50, 100 mg/K/day, dog, yielded non-specific toxicity only at 100 mg/K/day. 1459
Repeated skin tests at 1g/K, in oil solution, rabbit, Guinea pig, gave negative results. 1459
Transient irritation was observed in eye tests on rabbit. 1459
Non-sensitizing to the Guinea pig. 1459
Storage in tissues of rat and dog was insignificant. Sulfenone® is deemed to provide a wide margin of safety. 1459

2) Phytotoxicity:

a) Not recommended for use on pears (save Bartlett or D'Anjou), grapes, sensitive greenhouse plants, Cucurbitaceae, apple varieties susceptible to "russetting." 129, 1953
(1) Dusts are less phytotoxic than sprays, and organic solvents may enhance phytotoxic action and damage. 129
(2) Not phytotoxic for citrus fruits. 1698

3) Toxicity for acarines:

a) Structure and toxicity in substituted diphenyl sulfones: 900



R	R'	Concentration (%)	% Mortality, Metateranychus ulmi	
			Summer Eggs	Adults
(p-Chlorophenyl phenyl sulfone) 4-Cl	H	0.1	96.0	80.9
" "	"	0.025	75.9	65.6
H	H	0.1	98.1	69.3
"	"	0.025	83.3	63.1
4-Cl	4-Cl	0.1	0	—
"	"	0.025	—	54.1
4-Cl	4-CH_3	0.1	30.7	50.3
2,4-di-NO_2	4-CH_3	0.1	0	30.8
2-OH, 5-CH_3	2-OH, 5-CH_3	0.1	0	8.6
3-Cl, 4-OH	3-Cl, 4-OH	0.1	3.9	45.0
2-OH, 5-Cl	2-OH, 5-Cl	0.1	4.4	50.8
2-CH_3, 4-OH	2-CH_3, 4-OH	0.1	0	24.8
3-CH_3, 4-OH	3-CH_3, 4-OH	0.1	0	7.5
3-NH_2	3-NH_2	0.1	0	10.8

b) Sulfenone® vs. developmental stages of Tetranychus bimaculatus, placed on bean leaves treated in settling tower by method of Ebeling and Pence: 905

Formulation	LC_{50} (g/100 cc., 2 days post-treatment)			
	Adult	Larva	Egg	Adult On Leaf Surface Opposite to Treated Surface
Emulsion concentrate	.21	.23	.35	4.6
Wettable powder	.27	.26	.89	>5.0

c) Sulfenone® vs. Metatetranychus ulmi on Northern Spy apple, field tests, New York 1952; used as 50% wettable powder: 1990

Dosage/100 gallons	% Reduction In Mites After Spraying (July 4)		
	3 days	10 days	17 days
3 lbs	94.4	94.9	94.6
Control (no. mites hatched/leaf)	239	104	59

For comparison of Sulfenone® with other acaricides see Miticides or Acaricides, in this work.

d) Sulfenone® vs. *Septanychus texazona*, *Tetranychus bimaculatus*, on cotton plants; adult mites. Field tests of miscible oil concentrates, diluted with water, applied at 21.5 gal/acre: 2277

Lbs/acre Active Ingredient Required To Give
24 Hrs After Application

50% Mortality	95% Mortality	50% Mortality	95% Mortality
of *Septanychus texazona* (adults)		of *Tetranychus bimaculatus* (adults)	
0.478	3.659	1.712	90.49
(3 days after application)			
0.636	20.99	1.95	168.4
(5 days after application)			
0.435	7.38	1.108	83.03

Comparative effectiveness:

Days after application	Mite	Order (> = significantly more effective than)
1	*S. texazona*	parathion > Aramite® > Merthon > Sulfenone®
	T. bimaculatus	" " " " " " "
3	*S. texazona*	Aramite® > Sulfenone® > parathion = Merthon
	T. bimaculatus	Aramite® > parathion = Sulfenone® > Merthon
5	*S. texazona*	parathion = Aramite® > Sulfenone® > Merthon
	T. bimaculatus	parathion > Aramite® = Merthon > Sulfenone®

e) *Aceria sheldoni*: Poor to no control achieved, using emulsion concentrates and wettable powders of Sulfenone®.

f) Vs. *Tetranychus pacificus*, *Metatetranychus ulmi*, *Tetranychus bimaculatus*, *Bryobia praetiosa*, *Eotetranychus carpini borealis*, in apple orchards, Pacific Northwest, Sulfenone® 40-50% wettable powder at 2-3 lbs/100 gal gave poor control of *T. pacificus*, good control of the others with some inferiority (as compared with Ovotran®) for *E. carpini borealis*. 727

g) Effectiveness of Sulfenone® as a spray to control *Paratetranychus citri* adults on citrus trees, Southern California conditions: 1698

Orchard	Sprayed	Test Interval (days)	lbs/acre	Av. No. Adult Mites/ 32 Leaf Sample	
				Sulfenone®	Bis-(p-chlorophenoxy)-methane
Orange	March	11	3	18	1
"	"	11	6	23	—
"	"	11	12	27	—
"	"	20	4	44	1
"	"	20	8	37	—
"	"	20	12	12	—
"	August	93	4	4	5
"	"	133	5	99	35
"	"	133	10	12	—
Lemon	September	254	12	57	153
"	November	257	8	32	4
"	"	257	16	16	—
"	"	257	32	8	—
"	"	273	8	29	6
"	"	273	16	19	—

(1) Less effective than bis- (p-chlorophenoxy)-methane; 8-32 lbs/acre in late summer, fall gave fairly effective control of *P. citri*. Early spring treatments were less effective than bis-(p-chlorophenoxy)-methane, even at much higher dosages. Emulsible formulations were less effective than wettable powders.

h) Half life of Sulfenone® on citrus peel = 9-12 days. 1302

i) Sulfenone® vs. *Tetranychus bimaculatus*; T = topical treatment after which mites were transferred to untreated leaves; R = residue treatment with mites placed on treated leaves; TR = topical treatment, with mites allowed to remain on treated leaves: 904

Applied Via	Leaf	Formulation	LC_{50} (g/100cc) for *T. bimaculatus*		
			T	R	TR
Settling Tower	Bean	Emulsion	0.93	0.25	0.085
Settling Tower	Bean	Suspension	5.4	0.45	0.26
Settling Tower	Avocado	Emulsion	—	0.54	0.29
Settling Tower	Avocado	Suspension	—	0.6	0.48
Sprayer	Avocado	Emulsion	0.12	0.11	0.037
Sprayer	Avocado	Suspension	0.32	0.28	0.11

(1) Effectiveness, as residue (R as above), of Sulfenone® and others on bean and avocado leaves, treated in a settling tower; test organism = Tetranychus bimaculatus: 904

Compound	Formulation	LC_{50} (g/100cc) On	
		Bean Leaves	Avocado Leaves
Sulfenone®	Emulsion	0.25	0.54
Sulfenone®	Suspension	0.45	0.60
Parathion	Emulsion	0.0095	0.013
Parathion	Suspension	0.0072	0.0081
Aramite	Emulsion	0.0031	0.012
Aramite	Suspension	0.0035	0.014

37

CHLOROPICRIN (Trichloronitromethane; Nitrochloroform; Chlorpicrin.)

$CCl_3 \cdot NO_2$ Molecular weight: 164.39

GENERAL

(Also see Fumigants in this work)
[Refs.: 353, 129, 1953, 2815, 757, 1059, 314, 539, 605, 2260, 2669, 2668, 1711, 2949, 2826, 3343]

An insecticidal fumigant, first tested in the United States in 1917, its potential usefulness as an insecticide having been recognized in Austria in 1907. Toxic for man, it was used as a war gas in combination with more toxic vapors to induce vomiting. Sometimes added to other gases, for example methyl bromide, hydrogen cyanide, as a warning agent. Used in the fumigation of stored products and of the soil. On grain and other seeds it may be sprayed or poured directly and is often combined with carbon tetrachloride or ethylene dichloride to overcome the low volatility and promote vaporization. In the fumigation of grain or soil, chloropicrin is most effective in mixture with carbon tetrachloride at the rate of 1 pound chloropicrin to 1 gallon carbon tetrachloride. In soil fumigation, direct injection is the method of application although it is also emulsified in water and sprinkled on the surface or poured into borings.

Chloropicrin has a disadvantage in being retained by fumigated materials and requiring prolonged airing for removal. It is highly toxic to living plants, and may damage the germination potential of seeds. Hazardous residue levels may persist for from 1 hour to 1 week depending on temperature.

Chloropicrin is an effective weed killer, is effectively toxic for nematodes and fungicidal for many soil-borne pathogens with the exception of those forming sclerotia.

In closed top bins, chloropicrin may be applied by garden sprayer at 1.5-2 lbs per 1000 ft^3 to the space above the grain; mixtures of 20% chloropicrin and 80% methyl bromide may be similarly used. The latter mixture is especially useful in atmospheric vaults for fumigation of dried foods. Chloropicrin is also an extensively used local or "spot" fumigant. It has proved effective in controlling Japanese beetle grubs in the soil of nurseries, greenhouses and in quarantine treatment of potting material in plant-growing establishments. Useful in the protection of elevator-stored grains.

Chloropicrin is apparently toxic to all insects.

PHYSICAL, CHEMICAL

A colorless liquid, at room temperatures; non-flammable; of intense odor; exceedingly lachrymatory, nauseating, and vomitory, with extreme irritation of eyes, throat; m.p. -64°C; b.p. 112.4°C; $d_{4°}^{20°}$ 1.651 (as liquid), ca. 5.7 times as heavy as air; $n_D^{20°}$ 1.46; v.p. 5.7 mmHg at 0°C, 18.3 mmHg at 20°C, 23.8 mmHg at 25°C; vapor saturation at 25°C in mg/l = 212, 10 lbs/1000 ft^3 = maximum which can exist as a vapor at 68°F; bulk density: 275 cc = 1 lb, 13.8 lbs = 1 gallon; freezing point -69°C; soluble in water at 1 part: 400 parts at 0°C, 2.27g/liter at 0°C; soluble in alcohol, ether; non-corrosive, relatively inert chemically. Sufficiently irritating to be self-warning, thus reducing the toxic hazard; detectable at 1.25 ppm; lachrymatory at 2.4 ppm; sternutatory at 17 ppm; throat irritation at 11 ppm.

Formulations: Used alone or in combination with methyl bromide, ethylene dichloride, carbon tetrachloride, etc.

1) Maximum amount of chloropicrin which can exist as a vapor in a 1000 ft^3 fumigating chamber at various temperatures: 2621

Temperature(°F)	V.P. (mm Hg)	Maximum As Vapor (lbs/1000 ft^3)
32	5.7	3.4
59	13.8	8
68	18.3	10
77	23.8	13
86	31.0	17
95	40.0	21
104	51.0	27
113	65.0	34
122	81.0	42

a) 1 mg/l = 149.1 ppm; 1 ppm = .00671 mg/l. 2815

2) Sorption and penetration of chloropicrin by and through patent flour: 3013
   a) 78.3 mg sorbed by flour at 5 hrs exposure, 25°C, to 200 mg chloropicrin per liter at standard pressure; sorption ratio (CS_2= 1) = 7.2.
   b) 65.1 mg passed through patent flour after 24 hrs exposure at standard temperature, pressure; penetration ratio (CS_2 = 1) = 0.42.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage	Remarks	
Rabbit	ip	LD	500 mg/k	Death in 20 min—2 hrs.	2147
Rabbit	iv	MLD	10 mg/k		1173
Cat	sc	LD	ca10 mg/k		1173
Guinea Pig	inh	LC	0.8 mg/l, 110 ppm	Exposure 20 min; death in 2 days.	2656
Rabbit	inh	LC	0.8 mg/l, 110 ppm	Exposure 20 min; death in 3 days.	2656
Rabbit	inh	LC	5 mg/l, 742 ppm	Exposure continuous; death in 30 min.	2147
Cat	inh	LC	0.8 mg/l, 110 ppm	Exposure 20 min; death in 14 days.	2656
Dog	inh	LC_{50}	0.8 mg/l, 120 ppm	Exposure 30 min.	1665
Mammals	inh	LC	2 mg/l	Exposure 10 min.	2221
Mammals	inh	LC	0.05 oz/1000 ft^3	Exposure 10 min.	129
Mammals	inh	LC	2400 mg/m^3	Exposure 1 min.	129

a) Maximum concentration tolerated for 1 hour without serious symptoms (based on studies with Guinea pigs) = 1.0 ppm or 0.007 mg/l. 1665
b) Frequent exposure to sub-acute quantities enhances sensitivity to chloropicrin.
c) The extreme irritation aroused by chloropicrin in the pulmonary alveolar membranes may result in an edema which may prove fatal. 3343
d) Chloropicrin is an active inhibitor of sulfhydryl containing enzymes. 2231

2) Wildlife:

a) Even in low concentration, hazardous and generally toxic to most kinds of wildlife. 129

3) Phytotoxicity
   a) At properly applied insecticidal levels hazard may be controlled. 129, 353
   b) Very toxic when injected into soil and must not be applied near growing plants. 129, 353
   c) Said to injure seriously the germination capacity of radish and alfalfa seed. 353
   d) Apparently may be used safely in the fumigation of seed peas. 341

4) Toxicity for insects:
   a) Toxicity of chloropicrin for 8 species of stored products insects: 2005
      (1) Exposed at 70°F in 100 ft^3 empty fumatoria; adult insects:

Insect	Exposure 2 hrs		Exposure 6 hrs	
	LC_{50} (mg/l)	LC_{95} (mg/l)	LD_{50} (mg/l)	LC_{95} (mg/l)
Acanthoscelides obtectus	1.5	2.8	<1.5	<1.5
Oryzaephilus surinamensis	3.5	10.0	<1.5	3.2
Rhizopertha dominica	4.5	10.5	<1.5	2.6
Sitophilus granarius	16.0	34.5	3.4	8.0
Sitophilus oryzae	7.5	28.0	<1.5	3.9
Stegobium paniceum	5.5	16.0	1.9	3.4
Tribolium confusum	23.5	31.0	6.4	13.0
Zabrotes pectoralis	1.7	2.9	<1.5	<1.5

b) Other data, toxicity for insects, quantitative: (For comparisons of chloropicrin with other fumigants see Fumigants in this work)

Insect	Route	Dose	Dosage	Remarks	
Aonidiella (=Chrysomphalus) aurantii	Fumig	ca LC_{70}	8.8 mg/l	Exp. 25 min, 25° C; +1.5 mg/l HCN, 30% survival.	669
Aonidiella aurantii	Fumig	ca LC_{75}	10.0 mg/l	Exp. 25 min, 25° C; 25% survival.	669
Aonidiella aurantii	Fumig	ca LC_{90}	9.5 mg/l	Exp. 25 min, 25°C;+ 5% CO_2 8% survival.	669
Attagenus piceus (larva)	Fumig	LC_{50}	5.0 mg/l	Exp. 5 hrs, 25°C empty flasks.	2817
Attagenus piceus (adult)	Fumig	LC_{50}	1.3 mg/l	Exp. 5 hrs, 25°C empty flasks.	2817
Bruchus obtectus (adult)	Fumig	LC_{50}	$<$1.3 mg/l	Exp 5 hrs, 25°C flask fumigation.	2816
Cimex lectularius (egg)	Fumig	LC_{50}	4.613 mg/l	Exp. 5 hrs, 25°C, in 6.4 l flasks.	1292
Cimex lectularius (nymph 2,3 instar)	Fumig	LC_{50}	1.87 mg/l	Exp. 5 hrs, 25°C, in 6.4 l flasks.	1292
Cimex lectularius (adult)	Fumig	LC_{50}	2.233 mg/l	Exp. 5 hrs, 25°C, in 6.4 l flasks.	1292
Cimex lectularius (adult)	Fumig	LC_{95}	5.0 mg/l	Exp. 5 hrs, 25°C, empty flasks.	2622
Cimex lectularius (egg)	Fumig	LC_{95}-LC_{100}	$<$ 2.75 mg/l	Exp. 5 hrs, 25°C, in 12 l glass flasks.	2622
Cimex lectularius (older nymphs)	Fumig	LC_{95}-LC_{100}	5-6 mg/l	" "	2622
Cimex lectularius (adult)	Fumig	LC_{95}-LC_{100}	3 mg/l	" "	2622
Limonius californicus (larva)	Fumig	LC_{50}	0.7 mg/l	Relative toxicity (CS_2=1) 45.9.	1957
Limonius californicus (larva)	Fumig	LC_{100}	ca0.86 mg/l	" " " 45.9	1957
Limonius californicus (larva)	Fumig	LC_{50}	4.8 mg/l	Exp. 5 hrs, 77°F in 1 l flasks with 500 g soil.	1958
Limonius canus (larva)	Fumig	LC_{50}	4.8 mg/l	" " " " " "	1958
Oryzaephilus surinamensis (adult)]	Fumig	LC_{50}	1.4 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2816
Plodia interpunctella (larva)	Fumig	LC_{50}	2.25 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2817
Rhizopertha dominica (adult)	Fumig	LC_{50}	0.75 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2817
Sitophilus granarius (adult)	Fumig	LC_{50}	5.0 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2816
Sitophilus granarius (adult)	Fumig	LC_{99}	21.0 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2816
Sitophilus oryzae (adult)	Fumig	LC_{50}	2.0 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2816
Sitophilus oryzae (adult)	Fumig	LC_{99}	15.2 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2816
Tribolium castaneum (adult)	Fumig	LC_{50}	2.4 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2816
Tribolium confusum (egg)	Fumig	LC_{50}	45 mg/l	Exp. 5 hrs, 25°C, rel. humidity no > 10%.	2008
Tribolium confusum (egg)	Fumig	LC_{50}	16 mg/l	Exp. 5 hrs, 25°C, relative humidity 50-70%.	2008
Tribolium confusum (adult)	Fumig	LC_{50}	4.4 mg/l	Exp. 5 hrs, 25°C, relative humidity no > 10%.	2008
Tribolium confusum (adult)	Fumig	LC_{50}	4.4 mg/l	Exp. 5 hrs, 25°C, relative humidity 50-70%.	2008
Tribolium confusum (adult)	Fumig	LC_{50}	4.6 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2816
Tribolium confusum (adult)	Fumig	LC_{50}	5.0 mg/l	Exposed at 25°C.	156
Tribolium confusum (adult)	Fumig	LC_{50}	3.9 mg/l	25°C, 760 mm Hg no absorbing substance present.	1013
Tribolium confusum (adult)	Fumig	LC_{50}	35.5 mg/l	25°C, 760 mm Hg in presence of flour.	1013
Tribolium confusum (adult)	Fumig	LC_{99}	7.0 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2816
Tribolium confusum (adult)	Fumig	LC_{100}	2 oz/100 ft^3	Exp. 2 hrs, 72°F, empty tank fumigation.	607
Tribolium confusum (adult)	Fumig	—	48 oz/100 ft^3	Exp. 2 hrs, 72°F, 100% kill not achieved in tank filled with raw peanuts.	607
Tribolium confusum (adult)	Fumig	LC_{95}	4.0 mg/l	Exp. 5 hrs, 25°C, flask fumigation.	2816

c) Influence of temperature on the toxicity of chloropicrin for Tribolium confusum adults, exposed for 5 hrs. in empty fumigation flasks: 2816

Temperature (°C)	LC_{50} (mg/l)	LC_{99}(mg/l)
35	1.8	2.4
30	2.8	5.0
25	4.6	7.0
20	5.9	9.9
15	7.1	12.3
10	11.5	15.7
5	7.8	15.4
0	4.6	8.6

d) Minimum time of exposure of Tribolium confusum adults to chloropicrin at various temperatures, concentrations, for 100% mortality: 2996

Temperature (°C)	1 lb/1000 ft^3	2 lbs/1000 ft^3	3 lbs/1000 ft^3
35	1 hr 15 min	31 min	15-21 min
30	1 hr 45 min	35 min	25 min
25	2 hrs 15 min	50 min	30 min
20	2 hrs 15 min	1 hr 10 min	40 min
15	3 hrs 50 min	2 hrs	1 hr
10	4 hrs 30 min	2 hrs 40 min	1 hr 20 min

e) Relative susceptibility to chloropicrin of life cycle stages of *Tribolium confusum*, arranged from most susceptible to least susceptible: 2003, 2008

Larva > Adult > Pupa > Egg

f) Dosages of chloropicrin required to yield 100% kills of some stored grain insects in bagged grain: 1827

Insect	Dosage for 100% Mortality (lb/1000 ft^3)
Laemophoeus minutus	1
Rhizopertha dominica	1
Sitophilus granarius	1.5
Tribolium castaneum	3
The foregoing as mixed "population" + *Sitophilus oryzae*	3

g) Dosages of chloropicrin needed for 100% kills of *Tribolium castaneum* in wheat and other products in various types of container: 1827

Type of sack	Fumigation By Injection Method	Fumigation By Vault Method (24 hr exposure)
Pliofilm lined burlap	1 lb/1000 ft^3	—
Double paper lined burlap	3 lbs " "	> 3 lbs/1000 ft^3
Single paper lined burlap	> 8 " " "	.75 " " "
Cloth sacking (e.g. drill)	>11 " " "	.75 " " "

h) Post-fumigation (residual) effect of chloropicrin for *Tribolium castaneum* in wheat variously sacked: 1827

Type of sack	Injection Fumigation			Vault Fumigation (24 hr exposure)		
	dosage (lbs/1000 ft^3)	% kill after 4 days	% kill after 7 days	dosage (lbs/1000 ft^3)	% kill after 4 days	% kill after 7 days
Single paper lined burlap	7	24.5	100	0.25	52.6	92.3
Double paper lined burlap	1.5	40.4	100	.25	82.1	92.3
Pliofilm lined burlap	.75	0	100	3.0	90.5	100

i) Miscellaneous comments; Toxicity of chloropicrin for insects:

(1) *Tribolium confusum*, *T. castaneum*, *Sitophilus oryzae*, are more susceptible to chloropicrin when small amounts of CO_2 are added to the fumigant. 617

(2) For *Bruchus sinensis* chloropicrin was more toxic than hydrogen cyanide; for *Sitophilus granarius* it was 8-10 times as toxic as carbon disulfide. 2529

(3) For *Tribolium confusum*, *T. castaneum*, chloropicrin was 13 times as toxic as CS_2. 2816

(4) For *Musca domestica* chloropicrin, molecule for molecule, was 168 times as toxic as CS_2 (by wgt, 78 times as toxic as CS_2). 2996

(5) For wireworms (*Limonius* spp.), using the LC_{50} as basis, chloropicrin was 45.7 times as toxic as CS_2. 2816

(6) *Sitophilus oryzae* is much more susceptible to chloropicrin than *S. granarius*; larvae of *Hyponomeuta* were > susceptible than *Ephestia* larvae; ♂ *Blatta* > susceptible than ♀ *Blatta*. 2439

(7) Used successfully in control of *Odontria* in New Zealand. 1662

(8) For *Lasioderma serricorne*, neither at atmospheric nor reduced pressure could chloropicrin yield satisfactory control, and the fumigated tobacco products showed damage. 661

(9) For *Chironomus* spp. larvae, 8 ppm in water gave 100% mortality in 25 hours. 979

(10) For stored products insects in grain, chloropicrin, at 5 lbs per 1000 ft^3, was a powerful penetrating, fumigant, yielding high mortalities. 2221, 353

5) Pharmacological action; insects:

a) Classified as an irritant poison; believed to act by releasing acid in the tissues. 353, 3013

b) High concentrations immobilize *Tribolium confusum* in 30 seconds. 3013

38

CLOTHING IMPREGNANTS VS. CHIGGERS (TROMBICULIDS) 656

Compound	% Protection Offered After Launderings (No.) Shown										
	2	3	4	5	6	7	8	9	10	11	12
Benzil*	—	—	100	97	100	100	100	99	97	87	83
2-Thenyl salicylate	—	—	—	—	100	100	75	87	—	—	—
Diphenyl carbonate	—	—	—	—	100	100	99	79	—	—	—
Phenyl benzoate	—	—	—	—	100	100	98	0	—	—	—
2-Thenyl benzoate	—	—	99	100	98	100	92	0	—	—	—
Benzene hexachloride (12% γ)	—	—	92	39	—	—	—	—	—	—	—
Benzyl benzoate	100	99	—	—	—	—	—	—	—	—	—

* = 1,2-Diphenylethanedione, (diphenyl-α, β-diketone) $C_6H_5COCOC_6H_5$

39

COAL TAR DYES

1) Toxicity of some coal tar dyes which have been tested as toxicants for insects, by the leaf sandwich method: 455

Insect	Dye	LD_{50} Oral (mg/g)
Bombyx mori (4th instar)	Malachite green	0.025
" " " "	Safranin (bluish)	0.025-0.05
" " " "	Brilliant green	0.05
" " " "	Crystal violet	0.05-0.10

40

COPPER ARSENATE (BASIC.)

$Cu_3(AsO_4)_2 \cdot Cu(OH)_2$; $Cu(CuOH)AsO_4$; $4CuO \cdot As_2O_5 \cdot H_2O$ Molecular weight: 283

See, in this work, the section Arsenic Arsenicals, for consideration of general and common properties of arsenic and arsenicals as insecticides, comparative toxicity, pharmacology, modes of physiological action, etc.

PHYSICAL, CHEMICAL 3344

Gray-green, crystalline solid; occurs in nature as the mineral olivenite; contains 56.2% copper oxide (44.8% metallic copper), 40.6% arsenic pentoxide, 3.2% water of constitution. May be isolated in the pure state; stable; high insoluble in water (it dissolves to the extent of 3 mg As_2O_5, 0.05 mg Cu/liter); not subject to hydrolysis in water; slightly affected by presence of CO_2 (mixtures of 2 g/l in water, in presence of 0.2g CO_2, showed increase of soluble As_2O_5 from 0.15% to 0.35%, corresponding treatment of a basic calcium arsenate mixture, at 2 g/l, showed an increase of soluble AS_2O_5 from 0.8% to 10.4%); normal CO_2 content of air effects no detectable change in the soluble AS_2O_5 content of basic copper arsenate—water mixtures; dehydration of water of constitution requires heat of 700°C, the product of dehydration being copper oxyarsenate; by controlling temperature and rate of formation, basic copper arsenate may be produced in uniform particle size and shape, with crystals of 0.5 micra to 40 micra in size; particles of 1-3 micra are optimal in size for field use; grinding of the crystals in a mill enhances markedly the potential phytotoxicity; stable in the presence of lime at ordinary temperatures, but if boiled with lime a slight decomposition occurs, yielding calcium arsenate and black copper oxide; unlike acid lead arsenate, sodium chloride does not affect solubility; commercial preparations should contain not less than 22.5% As, and not more than 0.35% water soluble As, as the element.

TOXICOLOGICAL

1) Toxicity for higher animals: No data available to this compilation.

2) Phytotoxicity:
   a) Applicable to most types of vegetation, under ordinary conditions of temperature and humidity, without injury to foliage. 3238
   b) Not applicable to stone fruits, which are injuriously affected by all copper containing materials. 3238
      (1) Bean foliage was not injured in fog chamber experiments at saturation humidity, 72 hrs exposure, in contrast to acid lead arsenate which produced severe injury in 12 hours.
      (2) No injury to soybeans, under field conditions of high temperature, humidity.
      (3) No injury in the field, under conditions of high temperature and humidity, to field beans, cabbage, potatoes, tomatoes, grapes, apples.
   c) The low phytotoxicity is correlated with low availability of soluble As_2O_5. 3238
   d) Possesses marked toxicity for fungi.
   e) Heavy applications, as a dust, in boll weevil control, have rendered sandy loams unfit for cotton or other crops. 30 ppm total arsenic is the soil accumulation resulting from application of 50 lbs/acre/year. 618
   f) May be considered much safer to plants than other arsenicals, on the basis of the available water soluble As_2O_5. 3238
      (1) Air bubbled through a solution for 24 hrs yielded only 0.15% water soluble A_2O_5, while acid lead arsenate gave 0.8% or more and basic calcium arsenate gave 2-3%.

3) Toxicity for insects:
   a) As insecticidal as acid lead arsenate but has the advantage of high insolubility in water, thus reducing the phytotoxic hazard. 353
   b) Toxicity for insects is of the same general order as that of other arsenicals. 3238
   c) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Anticarsia gemmatilis (larva)	dust	LD_{50}	0.18 mg/larva	As effective as cryolite but better adhesion.	3238
Prodenia eridania (larva)	or	LD_{90}-LD_{100}	0.25-0.26 mg/larva		
Prodenia eridania (last instar)	or	LD_{50}	0.18-0.2 mg/larva	Acid lead arsenate 0.25-0.28 mg/g:	3238
Prodenia eridania (last instar)	dust		0.04,0.06 mg/cm^2	100% kill in 48 hrs of 400-500 mg larvae.	3238

   d) Toxicity as shown by field results:
      (1) Epilachna varivestis: At 1 lb/100 gallons yielded 100% control of larvae in 24 hrs; at 3 lbs/100 gallon gave 100% control of adults. 3238
      (2) Leptinotarsa decemlineata larvae: At 1, 2, 3 lbs per 100 gallons gave 100% kill of larvae in 1-2 days, depending on concentration. 3238

(3) Hyphantria cunea: At 3 lbs/100 gallons gave complete control in 48 hrs. 3238

(4) Ceratomia catalpae: At 3 lbs/100 gallons gave complete control in 48 hrs; equal to acid lead arsenate same strength for both H. cunea, C. catalpae. 3238

(5) Anticarsia gemmatilis: Used as a straight dust on soybean with excellent control. 3238

(6) Sulfur does not impair effectiveness of 25% copper arsenate dusts used to control Mexican bean and Colorado potato beetles. 3238

(7) Mexican bean and Colorado potato beetles: 3 lbs/100 gallons spray is recommended as the concentration to achieve control. Repels the potato leaf hopper. 753

(8) Protoparce sexta: Superior to DDT in the control of. 353

(9) Rhagoletis cingulata: Has been used in combination with sugar to control the cherry fruit fly. 2703

e) Miscellaneous comments:

(1) Larvae of Prodenia eridania fed longer on copper arsenate-dusted than on acid lead arsenate-dusted bean leaves; the average amount of copper arsenate consumed being 0.45 mg (1.8 times the LD_{90}-LD_{100} dosage of 0.25-0.26 mg/larva. Of acid lead arsenate the average amount consumed was 0.32 mg (only slightly above the LD_{90}-LD_{100} dosage of 0.3-0.31 mg). The insect, being sickened more slowly by copper arsenate, ingests a higher dosage before feeding stops. 3238

(2) The comparative toxicity of basic copper arsenate and acid lead arsenate, on the basis of 48 hour mortality readings corresponds, in approximate proportionality, to the As_2O_5 content (lead arsenate 30%, copper arsenate 40.6%.) 3238

(3) The toxicity of basic copper arsenate toward larval Prodenia eridania and Anticarsia gemmatilis, was enhanced by holding the insects at 60°F after feeding. The toxicity at 60°F holding temperature was twice that at 80°F, but mortality developed more slowly. 943

f) For screening test data consult Ref. 1801.

41

COPPER CYANIDE

1) Toxicity of copper cyanide for certain insects:

Insect	Route	Dose	Dosage	Remarks	
Bombyx mori (larva)	or	LD_{50}	0.037 mg/g		387
Ceratomia catalpae (larva)	or	LD_{50}	0.025 mg/g		387
Melanoplus differentialis	or	LD_{50}	0.13 mg/g		2617
Melanoplus differentialis	or	Lethal zone	0.21-5.8 mg/g	Survival time 57(18-107) hrs.	2617
Melanoplus differentialis	or	Intermediate zone	0.08-0.20 mg/g	" " 84(30-158) hrs.	2617
Melanoplus differentialis	or	Sublethal zone	0.03-0.07 mg/g		2617

a) Toxicity, as a dust, for Aedes aegypti larvae: 2848

Lbs/Acre	% Mortality After		
	1 day	2 days	3 days
0.5	47	73	87
0.06	30	40	65

b) Said to be equivalent in toxicity to Phenothiazine for control of Anopheles larvae. 2165

42

CRYOLITE (Sodium aluminum fluoride; Sodium fluoaluminate; Sodium aluminofluoride.)

$3NaF \cdot AlF_3$; Na_3AlF_6 Molecular weight: 210

GENERAL

[Refs.: 353, 2815, 757, 1059, 2104, 2221, 129, 1953, 1609, 484, 523, 2427, 436, 1221]

An insecticide employed as a stomach poison which, however, has marked contact insecticidal action. Extensively used in insect control since its introduction in 1929. Has now, like numerous other inorganic insecticides, been eclipsed and to a large extent replaced, by organic synthetic insecticides. The toxic properties of cryolite reside in its fluorine content.

Natural cryolite (ice-stone) is mined in Greenland, and imported into the U.S. The synthetic cryolite of similar composition shows little difference in effectiveness compared to the natural product. Large amounts have been used in control of codling moth, tomato pinworm, tomato fruitworm, corn earworm, Lima-bean pod borer, Mexican bean beetle, walnut husk fly, pepper weevil, blister, and flea beetles. Ordinarily applied as a suspension spray, but may be employed as a dust, diluted with talc, pyrophyllite, etc. or undiluted.

Attention is drawn to the section in this work on Fluorine, Fluorides, Fluosilicates, Fluoaluminates. There, the various properties of toxicological, pharmacological, and pharmacodynamic interest, shared in common by these substances as insecticides, are dealt with.

PHYSICAL, CHEMICAL

As a naturally occuring mineral, cryolite (ice-stone) contains 98% sodium aluminum fluoride. It may be synthesized from sodium chloride, ammonium fluoride and aluminum fluoride. Natural cryolite is a crystalline solid of monoclinic structure, the synthetic form is a white, amorphous powder; m.p. 1000°C; specific gravity 2.9; virtually insoluble in water (1 part [synthetic form] in 1629 parts water) 0.04-0.06% at 25°C, soluble in dilute alkali; pH of water suspensions: Imported product 3.6-6.1, American product 7.5-8.1; decomposed by alkalis, for example lime and Bordeaux mixture, with production of calcium fluoride; incompatible with alkaline materials, for instance lime-sulfur and Bordeaux mixture, either in the form of sprays or dusts.

TOXICOLOGICAL

1) Toxicity for higher animals; acute:

Animal	Route	Dose	Dosage	
Rat	or	LD$_{50}$ ca	200 mg/k	1951
Rat	or	MLD ca	40,000-50,000 ppm	2888, 728
Dog	or	Survived	13,500 mg/k	2102

a) Toxicity for rats of natural and synthetic cryolites; oral administration by catheter as cryolite-water pastes: 3027

Compound	Approximate Dosage (mg/k)	Sex	Result
Synthetic cryolite	< 200	♂	No adverse effect.
" "	200	♀	" " "
" "	500	—	" " "
" "	1000	♂	" " "
" "	2000	—	" " "
Natural cryolite	25	♂	" " "
" "	45	♀	" " "
" "	100	♂	" " "
" "	3300	♂	" " "
" "	5400	♂	" " "
" "	16,000	♀	" " "
" "	26,500	♂	" " "
" "	33,600	♀	" " "
Sodium fluosilicate (for comparison)	100	♀	" " "
" "	200	♀	" " "
" "	275	♂	Animal sick 3 days, recovery.
" "	375	♀	Death in 3 hours.
" "	400	♂	Death in 32 hours.
" "	(as dust on cage floor)		Death in 36 hours.

(1) May be considered of low toxicity for mammals.

2) Chronic toxicity for higher animals:

a) Rats die in 10 days on levels of fluoride ion at 900 ppm. To achieve this concentration with cryolite 40,000-50,000 ppm are necessary for an equitoxic effect. Disturbances of calcium metabolism underlie the chronic effects. 728

b) Chronic intoxication in experimental animals has followed the administration of 15-150 mg/k of various fluorides, fluosilicates and cryolite. 738

(1) The average acute LD as fluoride, for mammals, is ca. 0.5 g/k oral, 0.15 g/k subcutaneously, intravenously.

c) Tooth mottling in animals may follow prolonged intake of 2-3 ppm fluorine in drinking water. 1 ppm fluoride produces mottling of teeth in children. 25 ppm result in tooth striation in rats. 2880

3) Phytotoxicity:

a) Little phytotoxic hazard when used at proper insecticidal levels, for example at 0.2% for stomach and contact action. Cryolite has been considered the safest of the fluorine containing inorganic insecticides for use on plant foliage because of low solubility. 1953 2815

b) Orange trees withstand repeated application of 0.15% suspension as foliage spray. 2649

c) Used at 3000 lbs per acre on soil no adverse effects noted on Lima beans and bell peppers grown in treated soil. No deleterious effects on crops from soil accumulation of cryolite employed at insecticidal rates. 2795 129

d) Pome fruits, under conditions of cool, damp weather, may be damaged. 84

e) May seriously damage foliage and fruit of peach and plum trees both of which are unusually sensitive to cryolite. 2106

f) Seedling tobacco transplants, treated for root borer control by dipping of roots in 2.5% cryolite suspension, showed damage to 90% of the plants. 2797

4) Toxicity for insects: (an annotated bibliography, "The Fluorine Compounds as Insecticides", may be consulted in Ref. 486.)

Insect	Route	Dose	Dosage	Remarks	
Apis mellifera (adult)	or	LD_{50}	4.2 μg/bee	Particle size: Fine.	231
Apis mellifera (adult)	or	LD_{50}	5.5 μg/bee	" " Medium.	231
Apis mellifera (adult)	or	LD_{50}	13.0 μg/bee	" " Coarse.	231
Anticarsia gemmatilis (5th instar)	or	LD_{50}	0.17 mg/g (0.09-.25)	Av time for kill 20-48 hrs.	944
Ascia rapae (5th instar)	or	LD_{50}	0.68 mg/g (0.33-1.05)	" " " " " " "	944
Autographia brassicae (5th instar)	or	LD_{50}	0.42 mg/g (0.25-.77)	" " " " " " "	944
Bombyx mori (4th instar)	or	LD_{50}	0.05-0.07 mg/g		2819
Bombyx mori (4th instar)	or	LD_{50}	0.18 mg/g		459

a) Comparative toxicity of various fluoride-containing compounds for Bombyx mori (4th instar); oral administration: 459, 2819

Compound	LD_{50}, Oral (mg/g)
Cryolite, Na_3AlF_6	0.05-0.07
" "	0.18
Potassium fluoaluminate, K_3AlF_6	0.08-0.10
Ammonium fluoaluminate, $(NH_4)_3AlF_6$	0.11-0.14
Sodium fluoride, NaF	0.11-0.15
Manganese fluoride, MnF_2	0.20-0.40
Lead fluoride, PbF_2	0.25-0.40
Magnesium fluoride, MgF_2	>0.57
Sodium silicofluoride, Na_2SiF_6	0.10-0.13
" " "	0.09
Potassium silicofluoride, K_2SiF_6	0.07-0.10
" " "	0.13
Barium silicofluoride, $BaSiF_6$	0.09-0.12
" " "	0.17

b) Comparison of toxicities, and solubilities (in water) of various fluorine insecticides. Bombyx mori (4th instar): 2819

Compound	g/100 cc H_2O soluble at 25°C	LD_{50} Range, Oral (mg/g)
Cryolite	0.061	0.06
Potassium fluoaluminate	0.158	0.08-0.10
Sodium fluoride	4.054	0.11-0.15
Lead fluoride	0.066	0.25-0.40
Sodium fluosilicate	0.762	0.10-0.13
Potassium fluosilicate	0.177	0.07-0.10
Barium fluosilicate	0.025	0.09-0.12
Acid lead arsenate (for comparison)		0.086

c) Time required for 50% mortality among bees, Apis mellifera (adults) receiving orally 0.36% suspensions of cryolite: 812

Material	50% Mortality Time (Hrs)
Cryolite (natural)	8
" " + lime 1:1/2	20
" " " " 1:1	26
" " " " 1:2	35
" (synthetic)	4
" (natural) + Bordeaux 1:1	4
" " " " 1:2	4
" " + lead arsenate 1:1	8
" " filtered supernatant	23
" " 0.72% suspension	4

(1) 50% Mortality time, Apis mellifera, correlated with amount of fluorine present and the amount available; various fluorine-containing compounds and cryolite compared: 812

Material	Soluble In G/100 cc water (cold)	g Fluorine/100 cc (figures rounded) (0.36% Solution, Suspension)	50% Mortality Time (Hrs.)
Cryolite (natural)	0.36 @ 18°C	0.18	8
" (synthetic)	0.62 @ 18°C	0.19	4
NH_4HF_2	very soluble	0.24	1
NH_4F	" "	0.185	1 3/4
NaF	4.0 @ 15°C	0.163	4
KF	92.3 @ 18°C	0.178	4
NA_2SiF_6	0.652 @ 17°C	0.22	2 1/2
BaF_2	0.17 @ 10°C	0.08	8
CaF_2	0.0016 @ 18°C	0.175	—
$BaSiF_6$	0.026 @ 18°C	0.15	4

d) Comparison of the degree of control of certain economic insects using cryolite and Derris dusts: 3138

Derris dust		Cryolite Dusts			
% rotenone	% reduction of larvae	% Cryolite	Natural Cryolite With clay	Natural Cryolite With pyrophyllite	Synthetic Cryolite With pyrophyllite
			% reduction in larvae		
Mexican bean beetle (larva)					
0.5	99.8	50	99.8	98.1	92.0
.25	98.8	25	89.3	96.3	98.6
.125	96.9	12.5	88.5	90.7	82.9
.0625	80.5	6.25	79.8	88.5	48.9
Cabbage worm larvae					
0.5	59.2	50		66.4	80.0
.25	43.5	25		69.2	86.7
.125	46.7	12.5		73.3	64.2
.0625	33.6	6.25		60.0	42.5
Control	22.5			22.5	22.5
Potato flea beetles					
2.0	83.3	50	78.7		
1.0	80.1	25	76.3		
.5	82.5	12.5	79.4		
.25	68.7	6.25	68.7		
Control	58.4		58.4		
European corn borer (on potato plants)					
2.0	92.5	50	90.1		
1.0	73.1	25	66.9		
.5	54.1	12.5	70.2		
.25	45.8	6.25	25.2		

e) Hazard to beneficial insects:

(1) Said to be harmless to natural predators of orchard mites. 2039

(2) Used as a spray, at 3 lbs/500 gallons, on cotton the effect on beneficial Hippodamia convergens by one application method: 1450

Average kill of adults was 14% (7-23%)
" " " eggs was 4% (0-13%)
" " " larvae was 19% (9-28%)

Used as "Kalo" (natural cryolite with a sodium aluminum fluoride content of 90% [no less]) at 2 lbs per 50 gallons, the effect on Hippodamia convergens by one application method:

Average kill of adults was 4% (0-8%)
Average kill of eggs was 0
Average kill of larvae (1st instar) was 14% (6-14%)

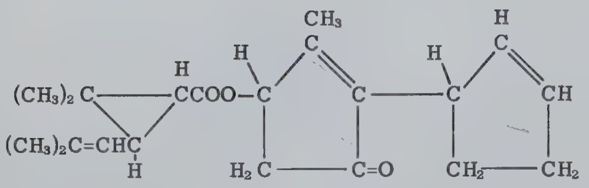
f) Resistance ("acquired") to cryolite among insects:
  (1) An enhanced resistance has appeared in "populations" of Rhagoletis completa (walnut husk fly) in the course of 9 years exposure to cryolite in field use in some parts of California. 2562
  (2) Certain exposed "populations" of Carpocapsa pomonella have revealed an enhanced resistance to the toxic action of cryolite. 1602

5) Pharmacological, pharmacodynamical, etc., insects:
  a) For a general treatment of pharmacology and pharmacodynamics, of fluorine containing insecticides for insects see, in this work, the section "Fluorides etc."
  b) Ingestion of cryolite by larval Prodenia eridania is followed by symptoms of marked sluggishness accompanied by spasm; death in flaccid paralysis finally ensues. 3349
  c) Cryolite is apparently toxic to most insects. 2104

6) Cryolite and insect control; field experiences: 199, 1355, 233
  a) The concentration to control Carpocapsa pomonella as a late season spray = 3 lbs/100 gal. 726, 2105
  b) Concentration to control Mexican bean beetle: 6 lb/acre as a dust. 2105
  c) Concentration to control Keiferia lycopersicella, Gnorimoschema operculella, Protoparce sexta, Heliothis armigera: 30 lbs/acre as a dust 40-70% strength or 6 lbs/100 gallons water as suspension spray. 2105
  d) Protoparce sexta is so resistant to DDT that cryolite stands out as an economical control insecticide; inferior however to toxaphene and DDD. 36, 37, 821
  e) For Anticarsia gemmatilis on peanut, soybean: As effective as DDT, BHC, Ryania. 110, 1873
  f) Prodenia litura control of, by cryolite, achieved in Queensland (Australia). 1264
  g) Argyrotaenia citrana: Inferior to DDD in control of. 2704
  h) Mineola vaccinii: Being replaced by Ryania, rotenone, in the control of. 229
  i) Diatraeea saccharalis: More effective than DDT, equal to Ryania, in the control of. 3287
  j) Pectinophora gossypiella: The inorganic insecticide of choice in the control of, although but 50% control is achieved. 160
  k) Acanthopsyche junodi: Superior to DDT in control of, 70% control vs 30%. 2492
  l) Pterandrus spp: Replaced by DDT and parathion in control of. 2649
  m) Chalcodermes aeneus: Inferior to DDT in control of. 3280
  n) Cylas formicaria (adults): Useful in control of. 561
  o) Anthonomus signatus: Controlled by, but cryolite inferior to DDT. 2143
  p) White fringed beetles: Effective against adults as full strength dust or spray at 1.5 ounces/gallon water. 353
  q) Reticulotermes flavipes: Effective, as soil treatment, in control of. 1855

43

CYCLETHRIN (DL-2-(2-Cyclopentenyl)-3-methyl-2-cyclopenten-4-o1-1-onyl DL-cis-trans-chrysanthemate; DL-Cyclopentenylrethronyl DL-cis-trans-chrysanthemate.)



Molecular weight: 328.534

GENERAL

A synthetic pyrethroid of considerable promise as an insecticide. (Also see Pyrethrins, Pyrethroids; Pyrethrum; Allethrin; Furethrin.) 1456

PHYSICAL, CHEMICAL

The technical product, 95% pure, is a brownish, viscous, oily liquid; $d^{0°}_{20°}$ 1.020; $n^{30°}_{D}$ 1.5170; insoluble in water; soluble in petroleum solvents, Freon®. A mixture of 8 isomers. 1456

TOXICOLOGICAL

1) Toxicity for insects:

a) Comparative toxicity of Cyclethrin, Allethrin, Pyrethrins, for Musca domestica as contact sprays; 1165

Substance	LC_{50} (Mg/Dl)	Relative Standard Error of LC_{50}, (%)
Cyclethrin	155.6	2.13
Allethrin	93.4	1.66
Pyrethrins	226.2	3.98

(1) Cyclethrin is 0.6 as toxic as allethrin, 1.5 times as toxic as pyrethrins, for Musca domestica (adult).

b) Mortality and "knockdown" of Musca domestica (adult) in tests using Cyclethrin, allethrin, pyrethrins alone and in synergism with piperonyl butoxide and sulfoxide. Space sprays applied by the turntable method: 1165

Substance	Concentration (Mg/Dl)		% KD	% Mortality
	Insecticide	Synergist	(In 25 min)	(In 1 day)
Cyclethrin	300	—	100	81.4
"	200	—	100	58.4
"	133.3	—	100	42.4
"	88.9	—	100	25.0
"	59.3	—	99.5	12.7
Allethrin	200	—	100	88.1
"	133.3	—	100	70.4
"	88.9	—	100	49.3
"	59.3	—	100	22.5
"	39.5	—	100	8.9
Pyrethrins	759	—	100	89.0
"	506	—	100	81.1
"	338	—	100	65.2
"	225	—	100	50.9
"	150	—	100	37.8
"	100	—	100	15.7
Cyclethrin+piperonyl butoxide	26.3	263	100	92.6
" " "	17.6	176	99.7	58.3
" " "	11.7	117	96.4	20.8
" " "	7.8	78	89.7	6.0
Allethrin+piperonyl butoxide	59.3	593	100	95.3
" " "	39.5	395	100	89.1
" " "	26.3	263	98.8	50.6
" " "	17.6	176	94.0	14.5
Cyclethrin+sulfoxide	26.3	263	100	89.1
" "	17.6	176	99.7	65.8

Substance	Concentration (Mg/Dl) Insecticide	Synergist	% KD (In 25 min)	% Mortality (In 1 day)
Cyclethrin+sulfoxide	11.7	117	97.6	20.3
Allethrin+sulfoxide	39.5	395	100	87.4
" "	26.3	263	99.7	50.6
" "	17.6	176	97.5	11.3
Pyrethrins+sulfoxide	12.5	125	100	74.7
" "	8.84	88.4	100	43.3
" "	6.25	62.5	100	15.5

c) Cyclethrin and synergists; effectiveness of vs. Pediculus humanus corporis in beaker tests: 390

(1) α-allylpiperonyl, α-propylpiperonyl, 4-(3,4-methylene dioxyphenyl)-sec.-butyl, α-allylisopropylpiperonyl esters of chrysanthemumic acid, have proved in these tests the most effective synergists of cyclethrin.

(2) Comparative: Pyrethrins + n-octyl sulfoxide of iso-safrole are more effective than cyclethrin with any synergist; allethrin + n-octylsulfoxide of iso-safrole is slightly less effective than cyclethrin + some of its better synergists; cyclethrin + n-octyl sulfoxide of iso-safrole in pyrophyllite dust formulations is slightly slower in "knockdown" action than allethrin and pyrethrins similarly synergised.

(3) Tabular evidence on the residual effectiveness of cyclethrin (per se) and cyclethrin + synergists in beaker tests. Materials applied to cloth patches and tested at various intervals (days) after application to cloth. Toxicant: Synergist ratio = 1 to 10:

Synergist	% Kill On Stated Day after Application To Cloth Initial	7 days	14 days	21 days	28 days	35 days	42 days
Acetic acid, phenyl-, α-isopiperonyl ester	100	100	90	85	75	50	—
Benzene, 1,2-methylenedioxy-4-[2-(octylsulfonyl) propyl]-chrysanthemumic acid-,	100	95	95	85	85	25	—
α-allylpiperonyl ester	100	100	100	100	90	85	75
α-cyclohexylpiperonyl ester	100	100	85	85	90	65	35
α-isopropyl piperonyl ester	100	100	100	100	100	100	90
4-(3,4-methylenedioxyphenyl)-sec.-butyl ester	100	100	100	100	100	100	85
α-(3-phenylpropyl)-piperonyl ester	100	100	65	45	—	—	—
α-propylpiperonyl ester	100	100	100	100	100	85	55
6-propylpiperonyl ester	100	95	70	75	70	35	—
Fencholic acid, α-allylpiperonyl ester	100	100	100	100	100	95	70
N-Isobutylundecyleneamide	65	15	—	—	—	—	—
MGK-264	100	100	95	100	100	35	—
Piperonyl butoxide	100	100	95	75	85	40	—
n-Propyl isome	100	95	80	65	35	—	—
Sulfoxide	100	95	70	75	75	70	5
Pyrethrins + Sulfoxide	100	100	100	100	100	100	100
Allethrin + Sulfoxide	100	100	90	100	95	45	—
Cyclethrin (alone)	5	—	—	—	—	—	—
Pyrethrins (alone)	20	—	—	—	—	—	—
Allethrin (alone)	10	—	—	—	—	—	—
Controls	5	0	0	0	0	0	0

(4) Cyclethrin and others, effectiveness, at various concentrations, per se and with Sulfoxide® as synergist:

Toxicant	% Kill At Concentration Indicated 0.005%	0.0025%	0.001%	0.0005%
Pyrethrins (alone)	20	10	—	—
Allethrin (alone)	40	10	—	—
Cyclethrin (alone)	0	—	—	—
Pyrethrins + Sulfoxide	100	100	40	25
Allethrin + Sulfoxide	100	100	65	10
Cyclethrin + Sulfoxide	100	75	40	15

44

CYTOCHROME OXIDASE, (EFFECT OF INSECTICIDES ON)

1) Effect of insecticides on the cytochrome oxidase of the coxal muscle of ♂ Periplaneta americana as measured by O_2 uptake in the Warburg apparatus: 2305

Insecticide	Molar Concentrations Tested
DDT	10^{-3}, 10^{-5}
DDD	10^{-3}, 10^{-5}
Methoxychlor	10^{-3}, 10^{-5}
Lindane	10^{-3}, 10^{-5}
Toxaphene	10^{-3}, 10^{-5}
Chlordane (cis-)	10^{-3}, 10^{-5}
Chlordane (trans-)	10^{-3}, 10^{-5}
Heptachlor	10^{-3}, 10^{-5}
Aldrin	10^{-3}, 10^{-5}
Dieldrin	10^{-3}, 10^{-5}
DNOC	10^{-3}, 10^{-5}
DNCHP	10^{-3}, 10^{-5}
DNBP*	10^{-3}, 10^{-5}
Nicotine	10^{-3}, 10^{-5}
Rotenone	10^{-3}, 10^{-5}
Ryania	"10^{-3}"
Sabadilla	"10^{-3}"
Pyrethrins	10^{-3}, 10^{-5}
Allethrin	10^{-3}, 10^{-5}
TEPP	10^{-3}, 10^{-5}
Parathion	10^{-3}, 10^{-5}
Schradan	10^{-3}, 10^{-5}
Malathion	10^{-3}, 10^{-5}
Phenothiazine	10^{-3}, 10^{-5}
Lethane 60	10^{-3}, 10^{-5}
Lethane 384	10^{-3}, 10^{-5}

*Dinitro-2-sec.-butylphenol.

a) Results:
- (1) All chlorinated hydrocarbons gave complete inhibition of cytochrome c oxidase at 10^{-3} M; slight transient stimulation at 10^{-5} M.
    - (a) Inhibition was rapid with DDD, methoxychlor, lindane, toxaphene.
    - (b) Inhibition was slow in onset with DDT, aldrin, dieldrin, chlordane.
- (2) Dinitro compounds were stimulatory at lower concentration; DNCHP, DNBP inhibitory at higher concentrations.
- (3) Organic phosphates, notably TEPP, stimulated at one or both concentrations tested; only parathion and malathion completely inhibited at 10^{-3} M concentration.
- (4) Nicotine stimulated at both concentrations.
- (5) Rotenone stimulated at 10^{-5} only.
- (6) Pyrethrins and allethrin inhibited completely at 10^{-5} M.
- (7) Phenothiazine, Lethane 60, Lethane 384 gave marked inhibition at 10^{-3} M.

45

D-D® (DD Mixture; Chlorinated propane-propylene mixture.)

$C_3H_4Cl_2$, $C_3H_6Cl_2$ (1,3-Dichloropropene [1,3-Dichloropropylene; 1,3-Dichloroprop-1-ene] + 1,2-Dichloropropane)

GENERAL

[Refs.: 1366, 129, 1953, 353, 1925, 491, 488]

A soil fumigant composed of chlorinated C_3 hydrocarbons, including 1,3-dichloropropene-1, 1,2-dichloropropane, and related compounds. The commercial mixture is stated to be 50% 1,3-dichloropropene, 25% 1,2-dichloropropane (propylene dichloride) 25% trichloro-, and tetrachloro-derivatives. A potent agent against soil nematodes. Effective in the fumigation of soils to control wireworms, garden centipedes, various mealy bugs, including pineapple mealy bug, grubs of *Anomala orientalis* and various scarabeid Coleoptera. Said to be less toxic to insects than ethylene dibromide. General toxicant for soil forms, best applied when the soil, at injection depths, has a temperature range of 40-80°F. 1,3-Dichloropropene has been considered by some to be the most toxic component, with the others having a possible synergistic action.

Soil application varies from 15-40 gallons per acre, with control of wireworms being achieved at ca. 25 gallons per acre. Toxic to mammals; hazardous.

PHYSICAL, CHEMICAL

At 77°F a liquid, dark brown to black in color, of pungent, garlic-like odor; moderately volatile; boiling range 122-129°F (approximate); $d_{20°}^{20°}$ 1.20 (average); bulk density (average) 10 lbs/gallon; flash point, tag closed cup, ca. 65°F; minimum chlorine content (% by weight) = 55.0; very slightly soluble in water; soluble in hydrocarbon solvents, halogenated solvents, esters, ethers, ketones; stable in presence of water, dilute acids, and salt solutions; reacts with dilute inorganic bases, concentrated acids, some metal salts, halogens, and active metals; moderately corrosive at room temperatures to aluminum containers; generally employed without mixing with other agricultural chemicals, and at full strength.

a) Properties of the chief ingredients: I) 1,3-dichloropropene: a mixture of 2 stereoisomers, α and β; b.p. α, β 108°C, α 104.2°C, β 112°C; $d_4^{25°}$ α, β 1.22, $d_{4°}^{20°}$ α 1.224, β 1.217; $n_D^{20°}$ α, β 1.4735, α 1.4682, β 1.4730. II) 1,2-dichloropropane: m.p. -70°C; b.p 95-96°C; $d_{4°}^{25°}$ 1.159; $n_D^{20°}$ 1.4388; molecular weight I = 110.98; II = 112.99.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   - a) Moderately toxic to mammals by ingestion or inhalation. The odor and irritant effects on the eyes and respiratory system warn of danger adequately and serve to minimize the hazard. 1366
   - b) Slightly toxic by absorption through skin. Very irritating to local skin areas. 1366
   - c) Toxic effects primarily local, in the area exposed. Hazard by ingestion and respiratory absorption: Moderate; by skin absorption: Slight. 1366
   - d) Human subjects experience acute distress of respiratory nature at more than 1500 ppm. 1366

Animal	Route	Dose	Dosage (mg/k, ppm)	
Mouse	or	LD_{50}	300 mg/k	1368
Rat	or	LD_{50}	140 mg/k	1368
Rat	inh	LC_{50}	1000 ppm	1368
Rabbit	ct	LD_{50}	2100 mg/k	1368

2) Chronic toxicity; higher animals:
   - a) Chief occupational hazards are: Skin contact, inhalation. The warning, irritant, effects of D-D® reduce the chronic exposure hazard. 1366

3) Symptoms of exposure:
   - a) Oral exposure is followed by acute gastrointestinal distress, with congestion and oedema of the lungs. 1366
   - b) Inhalation leads to gasping, refusal to breathe, and great distress at concentrations over 1500 ppm. Eye and upper respiratory irritation follow soon upon exposure to vapors. Repeated exposure may give rise to central nervous system depression. On cessation of exposure, symptoms soon disappear. 1366
   - c) Dermal exposure is followed by severe irritation, with marked cutaneous inflammation. 1366

4) Precautions, other remarks:
   - a) Precautions against swallowing, or exposure of skin and eyes, should be taken. Vapors should not be inhaled. Thorough washing after handling D-D®, and before smoking or eating, should be the rule. In case of prolonged exposure, as in handling and mixing operations, clean protective clothing, synthetic rubber gloves, masks or respirators, should be used. Contamination of food, or utensils for man or animals to be avoided. Keep away from children and domestic animals. 1366

b) If swallowed, spilled on skin or splashed into eyes, medical aid should be summoned. Meantime, the subject should be kept prone and quiet, exposed areas should be washed, contaminated clothing removed and not worn again until cleaned, or before complete evaporation of D-D®. Induce vomiting if D-D® has been swallowed. 1366

5) Hazard to wildlife; residue hazard:

a) It is stated that no hazard exists of D-D® is applied precisely as recommended by the producer. 1366

b) Dangerous residues are said to be absent from crops when the material has been used in the manner recommended. No removal methods are required or recommended. No tolerance levels have been established nor are they deemed necessary.

6) Phytotoxicity:

a) D-D® is toxic to plants and germinating seeds. In the fumigation of soils it should be used at least 15 days before planting, at an injection depth of 6-8 inches; a 3-4 week margin is even better. 1366 2820

(1) Stated to taint potatoes because of certain impurities which are present, i.e. 2,2-dichloropropane, 1,2,3-trichloropropane.

b) Soil accumulations to levels toxic for plants are not built up if the proper methods are used, even after several annual applications at excessive dosages. 1366

(1) Application is made at 10-90 gallons per acre before planting, according to soil conditions and pests to be controlled. Best results follow when soil temperatures, at injection depths, are between 40°-80°F with a moisture content sufficient for good seed germination.

(2) According to some, D-D® reduces the bacterial and fungal microflora of the soil. 1925

7) Toxicity for insects:

a) Toxicity values, as determined quantitatively for various insects, for the principal constituents of D-D® (1,3-dichloropropane, 1,2-dichloropropane [propylene dichloride]) may be found in the present work in the section Fumigants, General Treatment.

b) D-D® controls wireworms, for example, Limonius californicus, in soils, when applied at 26-36 gallons per acre. 1910 2991

(1) Mortality of Limonius californicus (larva), exposed in cages buried at various depths in soil. 1 ounce D-D® injected at 1 inch depth at corners of test areas 12-24 in^2; exposure 5 days. For comparison carbon disulfide, applied in same amounts and manner: 2990

Test Area Squares (Inches)	% Mortality			
	At 1-5 Inch Depth		At 5-17 Inch Depth	
	D-D®	CS_2	D-D®	CS_2
12	100	100	100	100
14	100	100	100	100
16	100	100	100	100
18	100	20	100	100
20	100	0	100	80
22	100	0	100	100
24	40	0	100	70
Control	5	0	5	0

(2) Mortality of Limonius californicus (larva), exposed in soil in 8 inch pots, treated with 1 quart of a solution of D-D® per 1 gallon water. 2990

	Mortality (%)	Exposure Time (Hrs)
	38.9	16
	66.2	24
	80.8	36
	91.1	48
	96.7	72
Control	2.5	

(a) Limonius californicus (larva), exposed in soil in 8 in. pots, treated with D-D® —water mixtures at various strengths; 1 quart of solution per experimental pot: 2990

cc D-D®/1 gal water	% Mortality
0.25	40
0.50	93.1
0.75	98.3
1.0	98.2
Control	2.5

c) Toxicity of D-D® mixture fractions, compared with D-D® mixture, propylene dichloride, chloropicrin, for Sitophilus oryzae: 488

D-D®		D-D b.p. 112°C		D-D b.p. 103-5°C		D-D b.p. 95°C		Propylene dichloride		D-D b.p.112°C 1% + Propylene dichloride 99%		Chloropicrin	
mg/l	% Kill	mg/l	%Kill	mg/l	%Kill	mg/l	%Kill	mg/l	%Kill	mg/l	%Kill	mg/l	%Kill
4.34	42	2.25	7	2.25	5	4.29	0	42.9	25	8.04	0	0.61	5
4.79	80	2.25	15	2.25	22	4.29	0	42.9	32	16.08	15	1.57	75
5.23	87	2.25	23	3.37	47	4.29	5	60.0	37	20.1	50	1.57	82
5.23	90	3.37	40	4.05	75	6.43	12	60.0	40	28.14	72	3.05	95
6.51	92	3.37	70	4.5	100	8.58	72	80.0	50	30.5	70	3.05	98
7.59	100	4.50	85	4.5	100	8.58	85	80.0	67	40.0	72	3.05	98
8.68	100	4.50	87			10.72	100	84.0	72	40.0	75	6.1	100
						21.4	100			40.0			
						42.9	100						
						60.0	100						
						77.0	100						

8) Pharmacological, pharmacodynamical, physiological considerations; insects:
   a) No available data.

9) Miscellaneous:
   a) D-D® has been reported as ineffective against the nematode Heterodera rostochiensis. 2482

46

DERRIS (Also see Rotenone, Rotenoids)

GENERAL

[Refs.: 2426, 1139, 353, 2231, 2815, 1059, 757, 1889, 1722, 1580, 2663, 1899]

Rotenone, and other rotenoids, present in the extractable resinous fraction, constitute the active principle of derris. However, the roots of certain rotenone bearing plants of the genus Derris, specifically Derris elliptica, Derris malaccensis, major sources of rotenone, may be used as an insecticide with no further treatment than drying, and suitable grinding, or pulverization. It is this natural product which is meant when the term derris is used in an insecticide context. By extension, the term may loosely be applied to other plants, which contain the same, or closely allied, active principles, namely, members of the genera Lonchocarpus, Tephrosia, Millettia, Mundulea, all of which, with Derris, belong to the family Leguminosae. In commerce, derris is also known as tuba root, a product, whole or ground, with a rotenone content of 4-5% on the average, which may, however, be as high as 13%. The terms cubé and timbo refer to the dried parts of Lonchocarpus utilis or Lonchocarpus urucu.

The insecticidal properties of Derris, and other rotenone bearing species, have long been appreciated among some peoples, e.g. the Chinese, and their use as fish poisons or stupefiants, is probably, among some peoples, very ancient.

Fundamental and critical studies of rotenone bearing plants have been carried forward by Tattersfield, and Tattersfield and Martin, and are to be found as a series in various volumes of the Annals of Applied Biology.

PHYSICAL, CHEMICAL

Since derris, in the sense of this treatment, is a complex substance and virtually in its natural state save for drying, grinding, or pulverization, a physical or chemical characterization, in the strict sense, is scarcely apropos. The following tabulation enumerates the insecticidally active compounds which have been isolated from derris, and lists some of their properties:

Compound	Empirical Formula	M.P. (°C)	% In Derris Resin	Insecticidal Activity (Relative)
Rotenone	$C_{22}H_{21}O_6$	163	2-40	100 (Standard)
Toxicarol	$C_{23}H_{22}O_7$	101	8-60	3
Deguelin	$C_{23}H_{22}O_6$	168	12-27	50
Sumatrol	$C_{22}H_{21}O_7$	188	0-15	7
Elliptone	$C_{19}H_{15}O_6$	159	?	20
Malaccol	$C_{19}H_{15}O_7$	244	?	?

a) The substance tephrosin, $C_{31}H_{26}O_{10}$, m.p.197, insecticidal activity (relative) 10 is an oxidation product.
b) Powdered derris (average particle diameter 6 μ) may be used as a suspension spray, as a dust with various inert diluents, adjusted to a rotenone content of 1%, and as impregnated dusts of dissolved derris resin absorbed on such carriers as pyrophyllite, diatomaceous earth, kieselguhr, walnut shell flour, kaolin, etc.

TOXICOLOGICAL

1) Fresh derris root is toxic, and suicide is possible by its use. The toxic properties of the bruised root for fish are both well-known and spectacular. 2815

2) Acute toxicity of powdered derris for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	350		1320
Rat	or	LD_{100}	400	Death in 24 hours.	52
Rat	or	LD_{70}	100	Sample containing 9.6% rotenone, 28.5% total extractives.	52
Rat	or	LD_{50} ca	1500		1951
Guinea Pig	or	LD_{100}	100	Death in 24 hours.	52
Guinea Pig	or	LD_{70}	75	Sample containing 9.6% rotenone, 28.5% total extractives.	52
Rabbit	or	LD_{100}	700	Death in 24 hours.	52
Rabbit	or	LD_{70}	600	Sample containing 9.6% rotenone, 28.5% total extractives.	52
Dog	or	LD_{100}	250	Death in 24 hours.	52
Dog	or	LD_{70}	150		52
Rat	or	LD_{70}	200	Cubé root, 4.7% rotenone, 21.4% total extractives.	1321
Guinea Pig	or	LD_{70}	200	" " " " " " "	1321
Rabbit	or	LD_{70}	1000	" " " " " " "	1321
Sparrow (Song, Chipping)	or	LD_{50}	120*		673
Sparrow (English)	or	LD_{50}	200*; 850**	Ground derris 25 times as toxic for birds	673
Robin (American)	or	LD_{50}	200*	as the pure rotenone (.75%) it contains.	673
Pheasant	or	LD_{50}	850*; 1200**	10 cabbage worms heavily dusted with derris would	673
Chicken	or	LD_{50}	1000*; 3000**	kill a young robin, 65 a young pheasant.	673
Fish	Medium	LD	0.2-2.0 ppm	[Refs.: 2751, 2899, 1335, 167, 1972, 1266, 168]	

* = Dosage for nestling birds; ** = dosage for older birds.

3) Chronic toxicity for higher animals:
   a) Rats, receiving derris powder (9.6% rotenone, 28.6% total extractives) in the diet at 78, 156 ppm for 150 days, grew normally; at 312 ppm growth was slightly retarded; at 1250, 2500, 5000 ppm the subjects died. 53
      (1) Livers of poisoned animals showed periportal lymphatic infiltration (mild to moderate), hyperemia and focal recrosis of the hepatic lobular midzone. Moderate glomerular and intertubular kidney hyperemia were noted.
   b) Growing dogs, receiving 400 ppm in the diet, showed stunted growths but adults were not affected by 240 days' exposure. 53
   c) Rabbits, receiving 30 mg/k/day for 30 days, showed no growth effects; 60 mg/k/day yielded a marked cumulative effect. 53
   d) Airborne dusts may prove an industrial hazard in derris processing. 1946

4) Pharmacological, pharmacodynamical, physiological:
   a) Derris is anaesthetic for vertebrate nerve. Respiration is affected, with a primary marked increase in rate followed by decline. Hypoglycemia in rabbits, dogs, has followed derris intake. 52
   b) Central nervous system action is particularly concentrated on the medulla oblongata. 464
   c) Administration to higher forms, by any route, produces vomiting. 1318
   d) Induces numbness and anaesthesia of oral mucous membranes, and, in contact with the eye, severe conjunctivitis.
   e) Intensely irritating to the skin and mucosae in rats. 52, 1859
   f) Cutaneous application does not lead to fatal outcome. 1949

5) Animal toxicity, miscellaneous:
   a) Toxic to aquatic invertebrates, particularly to Crustacea and to Protozoa. In the latter the symptoms of anoxia are noted. 3094

6) Phytotoxicity:
   a) Not phytotoxic. 1082

7) Toxicity for insects:
   a) For *Apis mellifera*, foraging among Lima bean plants in full bloom and dusted with derris is fatal. If dusting is carried on at times other than the blooming period application of dusts, with a rotenone content of 1.75%, is without hazard to honeybees. 996, 297
   b) The following insects are controlled by derris dusts: *Margantia histrionica*, *Nezara viridula* (slightly inferior to DDT, BHC, toxaphene in control of), *Epilachna varivestis* (superior to 10% DDT dusts in control of). No control of *Toxoptera gramineum* is effected by derris dusts of 1% rotenone content. 353

c) Comparative toxicity for *Musca domestica* of acetone extracts of *Derris* and *Lonchocarpus* diluted so as to give a root equivalent of 2 mg/cc; samples compounded to have a final rotenone content of 5%: 1728

Source	Concentrate (mg/cc)	Mean % Kill In 3 Days	Rotenone Equivalent Test Sol. (mg/cc)	Rotenone Equivalent Of Root (%)
Derris elliptica, Sarawak creeping.	2	57	0.28 ± .017	14.0 ± 0.85
Derris elliptica, Changi 3, low rotenone.	2	44	0.17 ± .012	8.5 ± 0.6
Derris elliptica, Changi 3, high rotenone	1	42	0.16 ± .011	16.0 ± 1.1
Lonchocarpus utilis	2	38	0.137 ± .011	6.9 ± 0.55
Lonchocarpus chrysophyllus	2	34	0.119 ± .010	6.0 ± 0.5
Rotenone	0.1	31	0.1 ± .01	5.0 ± 0.5
Rotenone	0.2	46	0.2 ± .016	10.0 ± 0.8
Rotenone	0.5	74	0.5 ± .035	25.0 ± 1.8

d) Derris, used either as ground root or extract, kills all attached ticks, *Ixodes ricinus*, on sheep, at dilutions down to 1 part (as resin) in 15,000 parts water in dip solutions. At a concentration of 1 part to 5000, it has an effective duration comparable to arsenic at 0.2% As_2O_3. Maximum effectiveness, as an emulsion wash, appears to endure about 14-17 days. 2071

e) Toxicity of derris resin for adult *Oryzaephilus surinamensis*: 2531

(1) Origin of resin: *Derris elliptica* (Changi). Spray in water + 5% saponin and 10% ethanol. Insects sprayed on bare glass dishes at 61°F, relative humidity 58.6%:

Conc. Resin* (mg/l)	% Mortality Av.Deposit=1.23 mg/cm²	Conc. Resin (mg/l)	% Mortality Av.Deposit=1.34 mg/cm²	Conc. Resin (mg/l)	% Mortality Av.Deposit =2.44 mg/cm²
CONTROL	0	CONTROL	4.9	CONTROL	2.86
10	0	40	14.5	20	23.5
20	4.8	60	43.8	40	56.8
40	1.6	80	59.7	50	69.1
80	25.4	100	92.2	60	94.3
120	53.9	120	86.3	70	96.9
160	78.3	160	96.3	80	100
240	96.4	240	100	100	96.3

* = Concentration In Resin.

f) For the overwintering larvae of the Clear Lake gnat, *Chaoborus astictopus*, derris powder, with a 5% rotenone content, at 1.0 ppm gave 98.3% mortality; 0.5 ppm yielded a mortality of 97.5% (concentrations were based on the rotenone content of the powder). 768

47

DIBUTYL ADIPATE (Di-n-butyl adipate; Experimental Tick Repellents 3 and 3 PS)

$C_4H_9OOC\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}CH_2COOC_4H_9$ Molecular weight: 222.318

GENERAL

[Refs.: 1953, 1801, 2120, 1249, 567, 1250]

An apparently safe repellent for ticks, when used for the impregnation of outer clothing at the rate of 1-2 g per ft² of cloth. Extensive screening tests indicate low insecticidal potential for lice (although fair ovicidal effect is indicated) mosquito larvae, fleas, ticks, cockroaches; low to absent "knockdown" effect for mosquito larvae, fleas, ticks; low, if any, repellency for mosquitoes, either when applied to skin or clothing; low flea repellency; rather high insecticidal and "knockdown" potential is indicated for chiggers, and high repellency for ticks both by "patch test" and "pen test." Repels ticks for several weeks from clothing which is infrequently worn. Used directly on dogs, repels the dog tick *Dermacentor variabilis* for from 1-2 days.

PHYSICAL, CHEMICAL

A colorless liquid; b.p. 183°C at 14 mm Hg; $d_4^{20°}$ 0.9652; virtually insoluble in water; miscible with alcohol, ether, as well as other organic solvents; an ester (of adipic acid) and thus incompatible with alkalis by which it is hydrolyzed.

Formulations: Experimental Tick Repellent 3 PS contains 15% by weight of the active ingredient with 85% propellants. In this form, it is sprayed directly on outer clothing. Experimental Tick Repellent 3 contains 90% of the active ingredient as an emulsifiable concentrate. This is diluted 1 volume to 16 volumes water as a dip for clothing, or a liquid to be applied directly to animals.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (g/k)	
Rat	or	LD_{50}	12.9 (9.9-17)	1250, 2908
Rabbit	ct	LD_{50}	> 20 cc/k	1250, 2908

2) Chronic toxicity to higher animals:

a) Dogs, receiving 23 applications (2 cc/k) in a period of 80 days showed slight desquamation of skin (some subjects) in regions of dense hair; weights remained normal. 1250

b) Rabbits, subjected to skin application (shaved skin) of cloth, impregnated with 1, 2 g/ft^2 dibutyl adipate, for 21 days showed no progressive damage following an initial erythema; animals normal 7 days later.

3) Effect upon ticks, repellency:

a) Impregnation of trousers and "coveralls" with an emulsion containing 90-100% di-n-butyl adipate gave protection from Dermacentor variabilis for several weeks when applied at 2 g per ft^2 of cloth (3 weeks for trousers, 7 weeks for "coveralls"). The repellent effect persisted through at least 2 washings. 1250

b) Trousers, treated with aerosols containing 5%, 15% di-n-butyl adipate with Freon® 11, 12 at the rate of 1-2 g per ft^2 of cloth, gave excellent repellency for Dermacentor variabilis for at least 3 weeks. 1250

c) Applied directly as an aerosol to dogs, fair protection toward Dermacentor variabilis was conferred for 1 day; reapplication every few days is necessary, and the nature of the formulation influences the repellency.

d) Repellency (field tests) vs. adult Dermacentor variabilis: Repellents applied to clothing at 2 g per ft^2 of cloth; tested 3 times, namely on the 2nd, 3rd, 4th weeks after treatment in exposures of 30 min—3 hrs (or until 25 ticks collected upon each of the controls): 1250

Repellent	% Repellency (Weeks Post-Treatment)			
	2 Weeks	3 Weeks	4 Weeks	Average
Di-n-butyl adipate	99	100	100	99.6
N-Butyl acetanilide (For Comparison)	89	80	96	88

e) Field and laboratory repellency tests of di-n-butyl adipate and allied compounds, applied to cloth and tested at 3 day and 3 week intervals after treatment: 1249

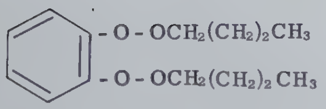
$$\% \text{ repellency} = \frac{\text{Number of ticks on untreated} - \text{Number of ticks on treated cloth} \times 100}{\text{Number of ticks on untreated cloth}}$$

Repellent	Field Trials				Laboratory Trials Vs. Amblyomma americanum
	Cloth Treated At 4g/ft^2		Cloth Treated At 2g/ft^2		% Repellency
	3 days (before test)	3 weeks	3 days (before test)	3 weeks	
	% Repellency For Dermacentor variabilis				
Dibutyl adipate	96.5	96.4	100	90	90
Dipropyl adipate	88.5	98.3	92	41	90
Diethyl adipate	84.0	57.0	67.5	70.6	50
Diallyl adipate	74.5	—	76	—	—
Dimethyl phthalate	78.5	37.6	73.6	53.5	50-75
Indalone*	77.5	67.5	53.5	69.2	50-70

* = Butyl mesityl oxide.

48

DIBUTYL PHTHALATE (Di-n-butyl phthalate; n-Butyl phthalate.)


- O - OCH$_2$(CH$_2$)$_2$CH$_3$
- O - OCH$_2$(CH$_2$)$_2$CH$_3$

Molecular weight: 278.34

GENERAL

[Refs.: 1801, 2919, 2715]

A repellent for ticks and a quick acting toxicant for certain trombiculid mites. Resists washing and is, therefore, an effective impregnant for cloth and clothing. Reported to be less effective in general repellency than the related dimethyl phthalate, q.v., but may be more effective against trombiculids; for example, chiggers. Stated to synergize with the pyrethrins.

Screening tests have indicated that dibutyl phthalate is ineffective as an insecticide, ovicide, or "knockdown" agent for lice, and equally ineffective, by the same criteria for fleas. Screening tests for killing and "knockdown" action for ticks (Amblyomma americanum) gave unimpressive results, but repellency, both by "patch" and "pen tests", was of a high order. Tested against the chigger, Trombicula splendens, dibutyl phthalate showed itself to be a fast acting toxicant, with high "knockdown" potential, rather than a repellent in the true sense. Mites were immobilized within at least 15 minutes. Effectiveness of treated cloth for trombiculids persisted through 3 or more standard washings on clothing treated with 2 g per ft^2. Tested against Aëdes aegypti, A. taeniorhynchus, A. sollicitans, Anopheles quadrimaculatus, for repellency in skin tests, dibutyl phthalate fell into the lowest class of effectiveness (0-30 minutes repellency time for A. quadrimaculatus, 0-60 minutes for A. aegypti. Likewise, in residual action against houseflies, dibutyl phthalate was in the lowest class, and for mosquitoes was but little better. Tested on Periplaneta americana as a 10% environmental dust in pyrophyllite, dibutyl phthalate ranged itself in the class of those substances giving 10-50% mortality in 48 hours.

The screening tests, in sum, confine the usefulness of dibutyl phthalate to the toxicant properties shown for trombiculids (chiggers) and as a tick repellent. Best used as a clothing impregnant.

PHYSICAL, CHEMICAL

Colorless to yellowish, viscous liquid; m.p. ca-35°C; b.p. 340°C; $d_4^{20°}$ 1.047; $n_D^{20°}$ 1.493; v.p. $<$0.01 mm Hg at 20°C. 1.1 mm Hg at 150°C; virtually insoluble in water (1 part in 2500 parts); soluble in most organic solvents e.g. alcohol, ether, acetone, benzene; viscosity 20.3 centipoises at 20°C; volatility 0.98 mg/cm^2/hour at 100°C; stable and inert, but hydrolyzed by alkalis.

TOXICOLOGICAL

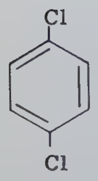
1) May be considered non-poisonous and generally non-irritating to human beings and animals.

2) Mouse ip LD_{50} 4140 mg/k 1748

3) Effective in the control of Amblyomma maculatum (Gulf coast tick) on livestock when compounded with 5% DDT and methyl abietate as an ear dressing or ointment. 2715

49

p-DICHLOROBENZENE (Paradichlorobenzene; p-Dichlorbenzene; PDB; Paracide; Di-Chloricide.)



Molecular weight: 147.01

GENERAL

[Refs.: 2295, 116, 932, 1501, 3199]

A fumigant of limited insecticidal use. Popular as a household fumigant for clothes moths and, for this purpose, is before the public in a multitude of guises. Has found some agricultural use as a soil fumigant for the peach tree borer and a number of other soil-dwelling forms. Has been reported as useful for the control of mites in cultures of fungi. Useful in the control of certain boring insects of shade and ornamental trees and large shrubs.

PHYSICAL, CHEMICAL

Colorless crystals or white crystalline masses; m.p. 53°C; b.p. 174°C; $d_{4°}^{20°}$ 1.458; $n_D^{69.9°C}$ 1.5266; v.p. 1.0 mm Hg at 25°C, 0.64 mm Hg at 20°C; flash point 67°C; virtually insoluble in water (79 ppm at 25°C) soluble in most organic solvents: Alcohol, benzene, chloroform, ether, carbon disulfide, being commonly used; vapor density 5 times that of air; stable; non-corrosive; sublimes at ordinary temperatures; 1 mg/l = 166.3 ppm, 1 ppm = 0.006 mg/l. Formulated as 100% crystals. Does not stain fabrics or other materials. 3199, 2221

a) Maximum weight of p-dichlorobenzene which can exist as a vapor in a 1000 ft³ fumigating chamber at various temperatures: 2621

Temperature (°F)	V.P. (mm Hg)	Lbs As Vapor/1000 ft³
32	.08	.04
59	.4	.2
68	.64	.3
77	1.0	.5
86	1.5	.7
95	2.3	1.1
104	3.4	1.6
113	5.1	2.4
122	7.4	3.4

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) To be considered no less toxic than benzene, although of low volatility. 1045

Animal	Route	Dose	Dosage	Remarks	
Rat	ip	LD_{50}	2562 mg/k	Given in oil.	3404
Fish	Medium	LC	50 ppm	Solubility at 25°C = 79 ppm.	754, 939
Mouse	or	LD_{50}	2950 mg/k		

b) Dogs have tolerated oral dosages of 15 g. 2922

c) Man has tolerated oral dosages to 20 g (300 mg/k) above which toxic effects appeared. 2815

d) Rabbits, exposed 30 minutes per day to 100 mg/l showed eye and nose irritation, muscular twitches, tremors, reflex impairment, nystagmus and rapid labored breathing; recovery occured in 0.5-2 hours after end of exposure. Granulocytopenia (with recovery in 3 weeks) was exhibited. 818, 3199

Rats, similarly exposed for 20 minutes per day showed primary irritation followed by total narcosis and later developed tremors and limb twitching enduring for 30-45 minutes after end of exposure; 40% of subjects developed granulocytopenia.

Guinea pigs, exposed to 100 mg/l, revealed signs resembling those above. However, repeated exposure produced intoxication so accentuated that many deaths occurred after a few exposures. All subjects lost weight and more than 50 % developed granulocytopenia.

Rabbits, repeatedly exposed 8 hrs per day to 4.6-4.8 mg/l (770-800 ppm) revealed tremor, weakness, nystagmus (sometimes), and some a transient oedema of the cornea; all subjects showed optic nerve-head oedema. Some died after a few exposures; a few only endured 62 exposures. None developed lens opacity. (With oral administration at 0.5 and 1.0 mg/k of naphthalene, in repeated dosage, cataracts were easily produced.)

e) Pathology
- (1) Rats, 0.005 g by subcutaneous route yielded occasional slight liver necrosis. 3199
- (2) Guinea pigs, exposed to vapors showed liver cell vacuolation; after repeated oral dosage: Hepatic vacuolization, necrosis. 3199
- (3) Pigs, fed corn containing PDB, exhibited cloudy swelling of liver cells, smooth muscle of spleen, larger arteries, tubular renal epithelium. Meat of animals was tainted in less than 15 days feeding, and 62 days was required after cessation of exposure for meat to become edible; weight gain of treated animals was impaired.
- (4) Man: Toxic and pathologic effects following exposure to PDB are recorded in some individual case histories reported by Ref. 3199.

2) Chronic toxicity, higher animals:

a) Prolonged and chronic, exposure to the vapors (1-2 year exposure) may lead to hepatitis, and even cataract 2815
of the eye. Prolonged contact with the vapors is to be avoided. Somewhat irritating to the skin. Does not 3199
sensitize guinea pigs.

3) Phytotoxicity:
- a) Vapor seriously impairs the germination capacity of even very dry seeds. 129
- b) Sprouting of fumigated "seed" sweet potatoes is decidedly retarded. 895
- c) Harmless to peach trees, when used as crystals in soil fumigation to control borers. 3374
- d) Used in oil emulsions (as a late summer foliage spray) may cause injury to plants. 116

4) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Musca domestica (larva)	Medium	LC_{50}	430.5 mg/100g food	LC calculated from dose-mortality curve.	2082
Musca domestica (larva)	Medium	LC_{50}	2880 ppm	Mixed in rearing medium.	356
Tribolium confusum*	Fumig	(approx) LC_{50}	.000078 moles/1	Exposure time 60 min gave 44% kill, 70 min gave 62% kill.	1956
Chironomus sp. (larva)	Medium	(approx) LC_{100}	6 ppm	Exposure 67-68 hrs to ortho-dichlorobenzene.	979

* Based on the exposure time required to kill 50% of the insects at atmospheric saturation, p-dichlorobenzene is 10-14 times less toxic than naphthalene.

a) Toxicity of p-dichlorobenzene for Musca domestica (3rd instar larvae), exposed to the combined stomach and fumigant action of the substance when mixed in the rearing medium; 240 individuals exposed to each concentration; mortality counted at 5 days: 2082

Concentration (mg/100g Medium)	% Mortality (5 days exposure)
99.9	0
149.8	5.2
249.4	14.7
497.5	54.9
744.4	84.9
990.1	95.4
1234.6	100.0

b) Pharmacological, pharmacodynamical, etc; insects:
- (1) In Periplaneta americana, p-dichlorobenzene produces symptoms characteristic of DDT and is considered primarily neurotoxic. 353
- (2) There is a marked and immediate increase in the O_2 consumption of the exposed intact, unrestricted insect. 2042
- (3) Considered to be a narcotic which increases the CO_2 output of insects. 2553
- (4) In advanced intoxication dissolves the somatic lipids. 3107
- (5) Administered by injection to Periplaneta americana, PDB produces tremors, followed, at length, by paralysis as is true of DDT. 2328

5) In the control of economic insects; field experiences:

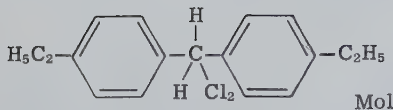
a) As a soil fumigant controlled the wintering nymphs of Eriosoma lanigerum. 2226
b) As crystals, or in emulsion, in a soil dressing at the base of trees at 0.75-1.0 ounces/tree controlled the 353
borer Aegeria exitiosa (=Sanninoidea). 2912
c) Melolontha vulgaris (larvae), controlled by. 1295
d) Used in control of Cyllene robiniae (locust borer) in 12% solution in 30% miscible pine oil. 1501
e) Used as sprays (in cottonseed oil) to combat Chrysobothris femorata and Cerambycid beetles. 1501
f) Used to control Musca domestica larvae in manure piles, latrines, refuse pits etc., where DDT is ineffective. In such situations it exerts, also, an ovicidal effect. Recommended by its penetrating qualities. Very effective also against blow-fly larvae in carcasses. 2166
g) Used effectively in the control of clothes moths at rate of 1 lb/100 ft^3. 396
h) Toxic to larvae of Agriotes spp; the ortho-form is likewise toxic, but the meta-form is but slightly so. 353

6) For screening test data, derived from use of p-dichlorobenzene against lice, mosquito larvae, chiggers and as a mosquito repellent consult Ref. 1801.

50

1,1-DICHLORO-2,2-BIS-(p-ETHYLPHENYL) ETHANE

(Perthane®; Di-(p-ethylphenyl) dichloroethane; 2,2-Bis-(p-ethylphenyl)-1,1-dichloroethane; Q 137 Experimental Insecticide)



Molecular weight: 307.254

GENERAL

[Refs.: 2693, 1576, 2120]

A compound related to DDT but which may be more specifically considered an analogue of DDD (TDE). It is recommended by an acute and chronic toxicity for mammals which is of a low order, compared with various other chlorinated hydrocarbon insecticides, yet it retains high toxicity for many insects. Commercial control of the following insects by Perthane®, on alfalfa and other forage crops, has been demonstrated by test: Leaf hoppers; on lettuce: 6 spotted leaf-hopper, cabbage looper; on apple: Wintering beet leaf-hopper, apple maggot, red-banded leaf roller. Promising results are reported in control of leaf hoppers, Egyptian clover weevil, Lygus spp., alfalfa caterpillar, cabbage looper, sugar beet leaf hopper, orange tortrix of citrus, sap beetle of corn, various leaf eating insects of cole crops; and household, livestock, fruit, and garden insects. Less insecticidally potent than DDT, but possesses some useful and promising specificities.

PHYSICAL, CHEMICAL

A solid of m.p. 56°-57°C. (No other precisions available.) Stable.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	9340 ± 120	Death in from 1-3 days.	1576, 1002
Mouse	iv	LD_{50}	173 ± 5	Death, save rarely, within a few minutes.	1576, 1002
Rat	or	LD_{50}	8170 ± 500	Death in from 1-4 days.	1576, 1002
Rat	iv	LD_{50}	73 ± 2	Death, save rarely, within a few minutes.	1576, 1002

a) For comparison the following acute oral LD_{50} values: Methoxychlor 6000; DDD 3400; DDT 250; Nicotine 50-60; rotenone 132; toxaphene 69; aldrin 67; parathion 3. (As mg/k for rats.)

2) Chronic toxicity for higher animals:

a) Rats, receiving over 2 year periods 0, 100, 500, 1000, 2500, 5000 ppm in diet: No effect on survival rate; initial depression in growth, disappearing after 6 months; no adverse haematological findings; no histopathological changes special to treated animals, save slight and infrequent hepatic tissue changes at the 2500, 5000 ppm, levels. 1576, 1002 2693

(1) Six week feeding of 50 ppm radioactive Perthane® in diet of 12 rats, showed storage in the body fat at a maximum of ca. 19 ppm, (1/10th the DDT storage potential under similar conditions).

b) Rabbits, receiving daily inunctions of Perthane® as a 30% solution in dimethyl phthalate, 5 days per week for 13 weeks (doses of 300, 900 mg Perthane®/k): No effects on survival or histopathological changes attributable to Perthane®. Some (minimal) skin irritation was observed on the shaved skin. 2693 1576 1002

c) Dogs (3 at each level), receiving 100, 1000, 5000 ppm in the diet: 1576, 1002

(1) Death ensued at the 5000 ppm level.

(2) At 100, 1000 ppm no effect on growth, survival; haematological picture normal.

(3) Cortical atrophy of the adrenals observed at 1000, 5000 ppm, but not at 100 ppm levels.

d) Dogs, fed (short-term tests) 200 mg/k/day (in capsules), became anorexic; killed at the end of the third week, adrenal cortical atrophy was shown by all. 1576 1002, 556

e) Dogs, receiving Perthane® as a 20% solution in corn oil by mouth at 200 mg/k/day, showed marked fall in the plasma 17-hydroxycorticosteroids which reached the zero level. One animal, recovering exceptionally slowly and killed at end of 4 weeks, revealed typical adrenal cortical atrophy; one highly sensitive subject showed a fall to zero of plasma 17-hydroxycorticosteroids after a single dose; one subject, receiving 6 doses, showed a zero 17-hydroxycorticosteroid level on the 5th day, and was dead on the eighth day. The experimental dogs were stimulated by adrenocorticotropic hormone.

f) Human subjects, subjected to a series of ten 24 hour patch tests with wool cloth patches Perthane® impregnated, and applied to different areas of skin in 25 individuals, followed after a 2 weeks rest by application 1576 of another pair of patches: No allergic responses, or reactions, developed in any subject.

g) Human subjects (50), exposed to aerosol Perthane® at 5 g/1000 ft³ for 7 minutes, showed no immediate or delayed reaction attributable to the test material. Individuals, working continuously or intermittently with Perthane® in the laboratory (in aerosol formulation) mixing fly spray mixtures for from 3 months to 2 years at concentrations varying from 0.25-10%, have shown no unusual physiologic response or dermal lesions.

3) Pharmacological, pharmacodynamical, physiological etc.:
   a) The adrenocortical manifestations associated with DDD and Perthane® have been mentioned above at "e".
   b) No specific data on the mode of action, etc., are available. Compare with DDT, DDD, and other related chlorinated hydrocarbons.

4) Phytotoxicity:
   a) No observations of phytotoxic effects on any plant species have come to the attention of this compilation.

5) Toxicity for insects:
   a) Quantitative:

Insect	Route	Dose	Dosage		Remarks	
Musca domestica	Topical(?)	LD$_{50}$	0.4-0.8	µg/insect	Route not specified.	1576
Prodenia eridania (larva)	Topical(?)	LD$_{50}$	2-3	µg/insect	Route not specified; 3rd instar.	1576
Chrysops discalis	Topical	LD$_{50}$ (estimate)	120	µg/fly		2707
Chrysops discalis	Topical	LD$_{90}$	400	µg/fly		2707

   b) Comparative toxicity Perthane® and other compounds for Chrysops discalis. Topical application: 2707

Insecticide	LD$_{50}$ (estimate) (µg/fly)	LD$_{90}$ (µg/fly)
Perthane® (Q 137)	120	400
Lindane	4	35
Endrin	9	80
DDT	20	250
Dieldrin	20	950
Methoxychlor	30	90
Aldrin	40	170
Heptachlor	40	200
EPN	48	120
Isodrin	60	170
Chlordane	60	650
Chlorthion	65	420
Diazinon	90	360
Malathion	130	330
Toxaphene	180	480

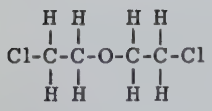
   c) Effect of Perthane® and other compounds on 3 species of beneficial insects. Adult insects placed on plants previously vacuum dusted with the insecticides: 1404

Dust and Concentration		% Mortality (24 Hrs)		
		Collops vittatus	Hippodamia convergens	Coleomegilla maculata
Perthane®	5%	23	6	12
DDT	5%	38	6	32
Strobane	5%	10	18	12
Heptachlor	2.5%	41	30	38
Toxaphene	10%	32	12	36
Endrin	1%	27	10	18
Dieldrin	2%	36	4	24
Parathion	2%	65	78	98
Malathion	5%	47	90	100
Chlorthion	5%	64	82	100
Diazinon	4%	37	66	100
Control		11	4	0
Lowest Significant Difference 5% level		20	24	26

6) Perthane® in practical insect control; field experiences: 1576
   a) At 2-5% in oil based sprays, aerosols, effective vs: Periplaneta americana, Blattella germanica, Blatta orientalis, Tineola bisselliella, Attagenus piceus, various ants of the family Formicidae; Lepisma saccharina, Musca domestica, Stomoxys calcitrans, Siphona irritans.
   b) At 1-2 lbs (active ingredient)/100 gallons, applied as emulsion, wettable powder, in regular spray schedules to fruit trees, effective vs.: Carpocapsa pomonella, Tachypterellus quadrigibbus, Conotrachelus nenuphar, Rhagoletis pomonella, Palracrita vernata, Alsophila pometaria.
   c) At 1-2 lbs/acre (active ingredient), effective vs: Spittlebugs, various Cercopidae, army worms, several Noctuidae, Lygus spp. (several), several Chrysomelidae, Loxostege spp., Autographa brassicae, Ascia rapae, Empoasca fabae, Epilachna varivestis.

51

DICHLOROETHYL ETHER (1-Chloro-2-(β-chloroethoxy) ethane; β,β'-Dichloroethyl ether; 2,2′-Dichloroethyl ether; sym.-Dichloroethyl ether; Dichlorethyl ether; Chlorex®.)



$$\mathrm{Cl{-}CH_2{-}CH_2{-}O{-}CH_2{-}CH_2{-}Cl}$$

Molecular weight: 143.02

GENERAL

[Refs.: 2670, 2120, 353, 2815, 1059, 757, 539]

In tests of the fumigant insecticidal properties of more than 300 aliphatic compounds for *Sitophilus oryzae*, dichloroethyl ether was among a limited number of outstanding fumigants. Although limited in uses as a space fumigant because of low volatility, it is recommended as a soil fumigant, especially valuable for greenhouse use. Toxic to most insects to a high degree. Also consult section entitled Fumigants.

PHYSICAL, CHEMICAL

A colorless liquid of pungent, irritating odor appreciable at concentrations of 0.0035% (v/v) in air, and highly lachrymatory at 0.05% (v/v) and above; m.p. -50°C; b.p.178°C; $d_4^{20^\circ}$ (as liquid) 1.22, (as a gas) 4.9 times as dense as air; $n_D^{20^\circ}$ 1.457; v.p. ca 0.73 mm Hg at 20°C, 1.1 mm Hg at 25°C; flash point 55°C; non-explosive; vapor saturation at 25°C = 23 mg/l; virtually insoluble in water (1.1 g/100 g H_2O at 20°C) soluble in most organic solvents; resists hydrolysis; powerful fat and lipid solvent. Vapors harmful, hazardous, but sufficiently self-warning; 1 mg/l = 171 ppm, 1 ppm = 0.00585 mg/l.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) At 10% concentrations or above must carry a warning indicating that it may be fatal if inhaled, swallowed or absorbed via skin by human beings. Vapors, or spray mists, are not to be breathed; contact is to be avoided, and contaminated clothing removed. Caution is recommended, in cases of concentrations below 10%, against inhalation, swallowing or skin contact. 3150
   b) Based on experiments with Guinea pigs, the maximum tolerated concentration for 60 minute exposure = 0.22 mg/l; for 8 hour exposures = 0.15 mg/l. The probable safe concentration for indefinite exposure is 0.1 mg/l, or 15 ppm, which is also the threshold limit. 1665, 55
   c) The odor is noticeable at 35 ppm, and nauseates at 100 ppm. The danger level for 30-60 minute exposure is 1000 ppm. 2780

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	136 (112-165)		2907
Rat	or	LD_{50}	105 (95-116)		2907
Rabbit	or	LD_{50}	126 (117-135)		2907
Rabbit	ct	LD_{50}	410 (350-480)		2907
Guinea Pig	inh	LC_{50}	5.9 mg/l, 1000 ppm	Exposure 45 minutes.	2910

(1) Guinea pigs tolerated exposures of several hours at concentration of 35 ppm without serious disturbances. 353

2) Phytotoxicity:
   a) Phytotoxic, and, as a soil fumigant, is to be used only on bare soils. 2120, 539
   b) Roses and carnations among others, are sensitive, and distinctly more susceptible than grasses. Seriously phytotoxic to young tobacco and dandelions. 353, 2634

3) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Limonius californicus (larva)	Fumig	LC_{50}	0.9 mg/l	Relative toxicity (CS_2=1)35; exposure in empty flasks.	1957
Limonius californicus (larva)	Fumig	LC_{100}	2.5 mg/l	Exposed in empty containers.	1957
Limonius californicus (larva)	Fumig	LC_{50}	272.6 mg/l	Exposure 5 hrs, 77°F, in soil.	1958
Limonius canus (larva)	Fumig	LC_{50}	272.6 mg/l	Exposure 5 hrs, 77°F, in soil.	1958
Periplaneta americana (adult) ♂	Contact	LD_0	.75 mg/g	Av. wgt. 0.9 (0.7-1.15)g (*)	2219
Periplaneta americana (adult) ♀	Contact	LD_0	.45 mg/g	Av. wgt. 1.3 (1.0-1.9)g (**)	2219

3) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Periplaneta americana (adult) ♂	Contact	LD_{50}	1.4 mg/g	(*)	2219
Periplaneta americana (adult) ♀	Contact	LD_{50}	0.8 mg/g	(**)	2219
Periplaneta americana (adult) ♂	Contact	LD_{100}	2.1 mg/g	(*)	2219
Periplaneta americana (adult) ♀	Contact	LD_{100}	1.2 mg/g	(**)	2219
Periplaneta americana (adult) ♂	or	LD_0	0.5 mg/g	(*)	2219
Periplaneta americana (adult) ♀	or	LD_0	0.2 mg/g	(**)	2219
Periplaneta americana (adult) ♂	or	LD_{50}	0.75 mg/g	(*)	2219
Periplaneta americana (adult) ♀	or	LD_{50}	0.35 mg/g	(**)	2219
Periplaneta americana (adult) ♂	or	LD_{100}	1.0 mg/g	(*)	2219
Periplaneta americana (adult) ♀	or	LD_{100}	0.5 mg/g	(**)	2219
Periplaneta americana (adult) ♂	inj	LD_0	0.38 mg/g	(*)	2219
Periplaneta americana (adult) ♀	inj	LD_0	0.18 mg/g	(**)	2219
Periplaneta americana (adult) ♂	inj	LD_{50}	0.55 mg/g	(*)	2219
Periplaneta americana (adult) ♀	inj	LD_{50}	0.25 mg/g	(**)	2219
Periplaneta americana (adult) ♂	inj	LD_{100}	0.8 mg/g	(*)	2219
Periplaneta americana (adult) ♀	inj	LD_{100}	0.4 mg/g	(**)	2219
Sitophilus granarius (adult)	Fumig	LC_{50}	1.7 mg/l	Exp. 5 hrs, 25°C, empty flask fumigation.	156, 2816
Sitophilus granarius (adult)	Fumig	LC_{99}(calculated)	3.7 mg/l	" " "	156, 2816
Sitophilus oryzae (adult)	Fumig	LC_{100} 48 hr	$<$ 24 mg/l	Exp. 24 hrs, 25°C, in 500 cc flasks with 200 g (ca 250 cc) wheat.	2670
Tribolium confusum (adult)	Fumig	LC_{50}	1.3 mg/l	Exp. 5 hrs, empty flask fumigation.	1798
Tribolium confusum (adult)	Fumig	LC_{50}	1.8 mg/l	Exp. 5 hrs, 25°C, empty flask fumigation.	156, 2816
Tribolium confusum (adult)	Fumig	LC_{99} (calculated)	3.5 mg/l	" " "	156, 2816

For comparison: Toxicity values for α, β-dichloroethyl ether

Limonius californicus (larva)	Fumig	LC_{50}	3.4 mg/l	Relative toxicity (CS_2=1) 9.2; flask fumigation.	1957
Limonius californicus (larva)	Fumig	LC_{100}	7.4 mg/l	Empty flask fumigation.	1957
Sitophilus granarius (adult)	Fumig	LC_{50}	1.7 mg/l	Exp. 5 hrs, 25°C, empty flask fumigation.	156, 2816
Sitophilus granarius (adult)	Fumig	LC_{99} (calculated)	4.7 mg/l	" " "	156, 2816
Tribolium confusum (adult)	Fumig	LC_{50}	2.1 mg/l	" " "	156, 2816
Tribolium confusum (adult)	Fumig	LC_{99} (calculated)	3.1 mg/l	" " "	156, 2816

For comparison: Toxicity values for chloromethyl ether

Tribolium confusum (adult)	Fumig	LC_{50}	3.3 mg/l	" " "	156, 2816
Tribolium confusum (adult)	Fumig	LC_{99} (calculated)	10.3 mg/l	" " "	156, 2816

For comparison: Toxicity values for sym.-dichloromethyl ether

Tribolium confusum (adult)	Fumig	LC_{50}	10.2 mg/l	Exp. 5 hrs, 25°C, empty flask.	156, 2816
Tribolium confusum (adult)	Fumig	LC_{99} (calculated)	14.2 mg/l	" " "	156, 2816

4) Pharmacological, pharmacodynamical, physiological:
   a) Action in insects is neurotoxic and narcotic, attended by a marked rise in O_2 consumption. 353
   b) The α, β-isomer is decidedly less toxic for wireworms and soil insects generally, than the β,β'-isomer. 1958

5) In the economic control of insects; field experiences:
   a) Conotrachelus nenuphar, successful control of larvae with 1.5% emulsions; pupae with 4.5% emulsions or 1 gallon emulsion/6 yards^2 of soil. Others report failure to control completely. 2913 514
   b) Successful use as fumigant and repellent, for wireworms. 465, 2989
   c) For control of "white grubs", Cotinus nitida, Phyllophaga horticula: poor control of 3rd instar larvae at 32 cc/gal H_2O rate of 1 gal/yd^2; excellent control of 3rd instar larvae at 32 cc/gal H_2O rate of 2-2 1/4 gal/yd^2. 2634
      (1) The emulsion contains Tergitol 7 and does no injury to blue grass, although it is severely injurious to small tobacco plants and dandelions.

6) Comparative toxicity, β, β'-dichloroethyl ether and other compounds:

   a) Action of various fumigants on Limonius californicus. Toxicity in empty flask fumigation; relative toxicities compared to carbon disulfide: 1957

Fumigant	LC_{50} (mg/l)	LC_{100} (approx)(mg/l)	Relative Toxicity(CS_2=1)
β,β'-Dichloroethyl ether	0.9	2.5	35
α,β-Dichloroethyl ether	3.4	7.4	9.2
Carbon disulfide	31.5	51	1.0
Methyl cyanide	55.8	86	0.56
Ethylene chloride	24.5	39.3	1.3
Ethyl formate	16.65	28.3	1.9
Diethyl carbinol	15.7	25.6	2.0

a) Action of various fumigants on Limonius californicus. Toxicity in empty flask fumigation; relative toxicities compared to carbon disulfide: 1957

Fumigant	LC_{50} (mg/l)	LC_{100} (approx)(mg/l)	Relative Toxicity (CS_2=1)
Methyl formate	12.5	23	2.5
Pyridine	5.9	15	5.3
Epichlorhydrin	0.8	2.4	39.8
Crotonaldehyde	0.74	1.1-1.3	42.4
Chloropicrin	0.7	0.86	45.9
Ethylene chlorohydrin	0.24	0.6-0.8	131.9
Allyl isothiocyanate	0.16	0.21-0.24	192.9

b) For Cimex lectularius, exposures 5 hours, at 25°C, in 12 liter glass flasks, empty: 2622

Fumigant	Approximate LC_{95}-LC_{100} (mg/l)		
	Older Nymphs	Adults	Eggs
α,β-Dichloroethyl ether	5-6	5-6	>6
HCN	0.4	<0.4	<0.4
Acrylonitrile	3-4	<2.5	2
Chloroacetonitrile	3-4	<3	<3
Chloropicrin	5-6	3	<2.75
1,1-Dichloro-1-nitroethane	8	<8	<8
Methyl bromide	9	<7	<7
Dichloroacetonitrile	10	<8	<8
Trichloroacetonitrile	11	8	<8
Ethylene oxide	14	6-10	<2
Methylallyl chloride	25-30	<25	<25
Ethyl formate	30	25-30	<25
sym.-Tetrachloroethane	35	35	25
Carbon disulfide	37.5	<30	30
Ethylene dichloride	>50	>50	>50
Carbon tetrachloride	>50	>50	>50
Trichloroethylene	>50	>50	>50

52

1,1-DICHLORO-1-NITROETHANE (Dichloronitroethane; Ethide®)

$CCl_2(NO_2)\cdot CH_3$ Molecular weight: 144

GENERAL

(Also consult the section entitled Fumigants in this work)
[Refs.: 353, 2120, 2815, 1059, 757, 2409, 2629, 2623, 1925]

A fumigant insecticide of comparatively recent introduction (1941). Suitable for the fumigation of stored products, bin fumigation of grain, etc., being effective against various stored products insects at 1-3 lbs per 1000 ft^3 at exposures of 24 hours. The undiluted material is absorbed on such materials as "Celotex," which are then placed, or suspended, in the upper reaches of the space to be fumigated. Dichloronitroethane is rapidly eliminated from fumigated materials by aeration. Has the property, valuable in any fumigant, of a self-warning, irritant, lachrymatory action. Related nitroparaffins share the valuable fumigant properties of dichloronitroethane. When used as a soil fumigant in compact soil, movement in the soil is at rate of 24 inches in 16 days (average of 1.5 inches/day); rate of movement is enhanced by soil loosening. Particularly suitable and effective in soil fumigation for wireworm control when temperatures are low.

PHYSICAL, CHEMICAL

A colorless liquid of distinct odor, lachrymatory, irritant; b.p. 124°C; $d_4^{20^\circ}$ 1.405; v.p. 16.9 mm Hg at 29°C; flash point (tag closed cup) 130°F; slightly soluble in water (1 part: 2500); soluble in most organic solvents or paraffinic substances; relatively inert but corrosive toward iron in presence of water; rapid in evaporation from surfaces. Vapors harmful to man, animals.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) Threshold limit for human beings = 10 ppm; odor and lachrymatory action, give adequate warning of appreciable concentrations. 55

Animal	Route	Dose	Dosage	Remarks	
Rabbit	or	LD	150-200 mg/k		2063
Rabbit	inh	LC_{100}	0.58 mg/l; 98 ppm	Exp. 300 min; death in several hrs.	2063
Rabbit	inh	LC_{100}	14.4 mg/l; 2445 ppm	Exp. 135 min; death in several hrs.	2063
Rabbit	inh	LC_{100}	57.7 mg/l; 9797 ppm	Exp. 10 min; death in several hrs.	2063
Guinea Pig	inh	LC_{100}	0.58 mg/l; 98 ppm	Exp. 300 min; death in several hrs.	2063
Guinea Pig	inh	LC_{100}	14.4 mg/l; 2445 ppm	Exp. 135 min; death in several hrs.	2063
Guinea Pig	inh	LC_{100}	57.7 mg/l; 9797 ppm	Exp. 10 min; death in several hrs.	2063

2) Toxicity for insects:

a) Concentrations for 100% kill of Tenebrio molitor (larvae), Tribolium confusum (adults), Sitophilus oryzae (adults): 1.5 lbs/1000 ft^3, exposure 1 hr at 26°C, 4 oz/1000 ft^3, exposure 8 hrs at 26°C. For insects buried in grain the dosages must be approximately double those given above. 2409

Insect	Route	Dose	Dosage	Remarks	
Cimex lectularius (older nymphs)	Fumig	approx LC_{95-100}	8 mg/l	Exp 5 hrs, 25°C, 12 l fumigation flasks, empty.	2622
Cimex lectularius (adults, eggs)	Fumig	approx LC_{95-100}	<8 mg/l	" " "	2622
Dacus dorsalis (eggs)	Fumig	LC_{50}	24 mg/l	Exp 2 hrs, 71-80°F, empty vessel; naked eggs.	255
Dacus dorsalis (eggs)	Fumig	LC_{95}	60 mg/l	" " "	255
Dacus dorsalis (larvae, 3rd instar)	Fumig	LC_{50}	<1.9 mg/l	" " "	255
Dacus dorsalis (larvae, 3rd instar)	Fumig	LC_{95}	<1.9 mg/l	" " "	255
Sitophilus granarius (adult)	Fumig	LC_{50}	4.9 mg/l	Exp 24 hrs, 80°F at surface of	2009
Sitophilus granarius (adult)	Fumig	LC_{95}	9.8 mg/l	" " wheat in 28 liter cans 14.5 in	2009
Sitophilus granarius (adult)	Fumig	LC_{50}	7.3 mg/l	" " buried 2 high, 12.5 in. diameter con-	2009
Sitophilus granarius (adult)	Fumig	LC_{95}	12.2 mg/l	" " inches in taining 30 lbs whole wheat	2009
Sitophilus granarius (adult)	Fumig	LC_{50}	11.1 mg/l	" " buried 5 grain 8 inches deep; 6.5 in	2009
Sitophilus granarius (adult)	Fumig	LC_{95}	21.7 mg/l	" " inches in free space above wheat.	2009
Tenebrioides mauritanicus (adult)	Fumig	LC_{50}	0.019cc/5 lb v/v, 0.027g/5 lb w/w	Exp 24 hrs, 30°C, in 5 lb lots of shelled corn.	2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{95}	0.024cc/5 lb v/v, 0.034g/5 lb w/w	" " " " "	2603
Tribolium confusum (adult)	Fumig	LC_{95}	12 mg/l	Exp 5 hrs, 25°C, static fumigation, empty flasks.	2629, 2632
Tribolium confusum (adult)	Fumig	LC_{50}	9 mg/l	" " " " "	2629, 2632
Tribolium confusum (adult)	Fumig	LC_{50}	7.9 mg/l	Exp 24 hrs 80°F at surface of	2009
Tribolium confusum (adult)	Fumig	LC_{95}	13.2 mg/l	" " wheat in 28 liter cans 14.5 in	2009
Tribolium confusum (adult)	Fumig	LC_{50}	15.5 mg/l	" " buried 2 high, diameter 12.5 inches	2009
Tribolium confusum (adult)	Fumig	LC_{95}	22.5 mg/l	" " inches in containing 30 lbs whole wheat	2009
Tribolium confusum (adult)	Fumig	LC_{50}	17.3 mg/l	" " buried 5 grain 8 inches deep; 6.5 inches	2009
Tribolium confusum (adult)	Fumig	LC_{95}	30.1 mg/l	" " inches in free space above wheat.	2009
Thermobia domestica	Fumig	LC_{50}	1.33 mg/l	Exp 5 hrs, 30°C, in 5.5 l flasks.	1261
Thermobia domestica	Fumig	LC_{90}	2.62 mg/l	" " "	1261
Thermobia domestica	Fumig	LC_{50}	2.8 mg/l	Exp 2 hrs, 30°C, in 5.5 l flasks.	1261
Thermobia domestica	Fumig	LC_{90}	4.4 mg/l	" " "	1261
Oryzaephilus surinamensis	Fumig	LC_{50}	2.75 mg/l	Exp 5 hrs, 30°C, in 5.5 l flasks.	1261
Oryzaephilus surinamensis	Fumig	LC_{90}	4.44 mg/l	" " "	1261
Callosobruchus maculatus	Fumig	LC_{50}	2.01 mg/l	" " "	1261
Callosobruchus maculatus	Fumig	LC_{90}	3.47 mg/l	" " "	1261
Rhizopertha dominica	Fumig	LC_{50}	2.23 mg/l	" " "	1261
Rhizopertha dominica	Fumig	LC_{90}	3.47 mg/l	" " "	1261

(1) 100% mortalities of larvae of Tenebrio molitor, adults of Sitophilus oryzae, adults of Periplaneta americana, freely exposed (empty space) to vapors at 26°C, were obtained as follows: With 1.5 lbs per 1000 ft^3, 2 hour exposures; with 1 lb per 1000 ft^3, 3 hrs exposures; with 8 oz per 1000 ft^3, 4 hrs exposures; with 4 oz per 1000 ft^3, 8 hrs exposures. With the foregoing insects buried at the center of 100 lb bags of wheat grain, the following dosages and exposure times were required to yield 100% mortality: 3 lbs per 1000 ft^3, exposure 4 hrs; 2.5 lbs per 1000 ft^3, exposure 6 hrs; 2 lbs per 1000 ft^3, exposure 8 hrs; 1.5 lbs per 1000 ft^3, exposure 10 hrs; 1 lb per 1000 ft^3, exposure 12 hrs. 2409

b) Toxicity of some related nitroparaffins for various insects:

(1) 1,1-Dichloro-1-nitropropane: $CH_3CH_2CCl_2NO_2$:

Insect	Route	Dose	Dosage	Remarks	
Tribolium confusum (adult)	Fumig	LC_{50}	8 mg/l	Exp. 5 hrs, 25°C, static fumigation, empty flask.	2629, 2625
Tribolium confusum (adult)	Fumig	LC_{95}	11 mg/l	" " " " "	2629, 2625

(2) Toxicity of other nitroparaffins as fumigants for various insects:

Nitroparaffin	Insect	Dose and Dosage	Remarks	
1-Nitrobutane $CH_3(CH_2)_3NO_2$	Tribolium confusum	LC_{50}=8 mg/l, LC_{95}=10 mg/l	Exp 5 hrs, 25°C, empty fumigation flasks.	2625
"	Cimex lectularius	LC_{95}=32 mg/l		2622
Nitroethane $CH_3CH_2NO_2$	Tribolium confusum	LC_{50}= 8 mg/l, LC_{95}=14 mg/l	" " "	2625, 2632
"	Cimex lectularius	LC_{95}=32 mg/l	" " "	2622
1-Nitropropane $CH_3(CH_2)_2NO_2$	Tribolium confusum	LC_{50}=11 mg/l, LC_{95}=16 mg/l	" " "	2625
"	Cimex lectularius	LC_{95}=20 mg/l	" " "	2622
2-Nitrobutane $CH_3CHNO_2CH_2CH_3$	Tribolium confusum	LC_{50}=13 mg/l, LC_{95}=20 mg/l	" " "	2625

Nitroparaffin	Insect	Dose and Dosage	Remarks	
2-Nitropropane $CH_3CHNO_2CH_3$	Tribolium confusum	LC_{50}=19 mg/l, LC_{95} 35 mg/l	Exp 5 hrs, 25°C, empty flasks.	2625
Nitromethane CH_3NO_2	Tribolium confusum	LC_{50}=37 mg/l, LC_{95}=55 mg/l	" " "	2625
For Comparison:				
Carbon disulfide	Tribolium confusum	LC_{50}=56 mg/l, LC_{95}=100 mg/l	" " "	2625

c) Comparative toxicity, dichloronitroethane and other fumigants:

(1) Dosages of various fumigants required for 95% mortality of Tribolium confusum and Sitophilus granarius, exposed at the least effective level (5.5 inches) in wheat grain (other positions tested: surface, 2 inch depth) in 28 liter cans, 14.5 inches high, diameter 12.5 inches, containing 30 lbs whole grain wheat 8 inches in depth, with 6.5 inch free space above the grain surface: 2009

Fumigant	Tribolium confusum		Sitophilus granarius	
	mg/l	cc/0.5 bushel	mg/l	cc/0.5 bushel
1,1-Dichloro-1-nitroethane	30.1	0.59	21.7	0.43
Methyl bromide	5.3 (least effective at surface)	0.09	3.9	0.06
Acrylonitrile	19	0.67	6.8	0.24
Ethylene chlorobromide	28	0.46	39.1	0.65
Methylallyl chloride	29.5	0.89	15.0	0.45
Ethylene oxide	30.0	0.95	14.3	0.45
Hydrogen cyanide	39	1.6	60.4	2.5
Carbon disulfide	54	1.2	43	0.95
Ethylene dibromide	56	0.72	60	0.77
Carbon tetrachloride	110 (least effective at surface)	1.90	230	4.04
Ethylene dichloride	111	2.5	> 200	4.46

(2) Fumigants for Tenebrioides mauritanicus, exposed in 5 lb lots of shelled corn for 24 hrs at 30°C; adult insects: 2603

Fumigant	LC_{50}		LC_{95}	
	cc/5 lbs Corn	g/5 lbs Corn	cc/5 lbs Corn	g/5 lbs Corn
1,1-Dichloro-1-nitroethane	0.019	0.027	0.024	0.034
Ethylene dibromide	.2	.043	.036	.078
Carbon disulfide	.102	.129	.111	.104
Methylbromide + CCl_4 1:9 v/v	.120	.191	.161	.256
β-Methylallyl chloride	.131	.121	.208	.192
" "	.108	.100	.191	.177
Carbon tetrachloride	.276	.438	.455	.723
1,1,2-Trichloroethane	.352	.508	.566	.817
Ethylene dichloride	.467	.585	.903	1.135

(3) Comparative toxicity dichloronitroethane and other compounds for Tribolium confusum; exposures 5 hrs, static fumigation at 25°C in empty flasks; 50-75 insects/test; 6-8 tests/fumigant. Mortality data taken 20-21 days post fumigation: 2629

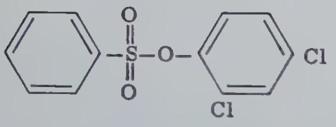
Fumigant	Approximate Concentration For 50% mortality (mg/l)	95% mortality (mg/l)	
1,1-Dichloro-1-nitroethane	9	12	
1,1-Dichloro-1-nitropropane	8	11	
Chloroacetonitrile	< 2	< 3	Death in 6 hours.
Acrylonitrile	> 2	< 3	" " " "
Methylbromide	ca 8	ca 11	
Ethylene dichloride	6	12	
Ethylene dichloride + CCl_4 3:1	9	14	
Methylallylchloride	12	19	
Methylallyl bromide	14	—	
Ethylene oxide	< 20	< 25	
Carbon disulfide	56	100	
Ethyl bromide	> 150	< 200	

(4) Data on screening tests may be found in Ref. 1801.

53

2,4-DICHLOROPHENYL BENZENE SULFONATE

(Genite®; Genite 923 of Allied Chemical
and Dye Corporation)



Molecular weight: 319.16

GENERAL

[Refs.: 353, 2231, 191, 291, 1698]

Reported to be an effective residual acaricide, but with a tendency to phytotoxicity for the foliage of orchard trees. Stated to be approximately one third as ovicidal for Tetranychus telarius as p-chlorophenyl benzene sulfonate, q.v. Also, consult the section of this work titled Miticides or Acaricides. In a four grove test (orange, lemon trees) found to be inferior to bis-(p-chlorophenoxy) methane, q.v.

PHYSICAL, CHEMICAL

Technical: A tan, waxy solid; m.p. 46-47°C; specific gravity 1.39; insoluble in water, soluble in most organic solvents and aromatic oils; stable in presence of weak alkalis, and in oil solutions.

TOXICOLOGICAL

1) Acute toxicity for higher animals: No data available; for precautionary labelling see Ref. 3150.

2) Toxicity for Acarina:
   a) Tested in the control of Paratetranychus pratensis on wheat under New Mexico field conditions, Genite® (tested as Compound 923) was unable, among others, to achieve control with as high as 75% mortality. 1442
   b) In field tests for the control of Aceria sheldoni, 2,4-dichlorophenyl benzene sulfonate used as emulsions or wettable powders, on citrus trees achieved poor to no control, (preliminary trials). The failure was shared by numerous other acaricides and acaricide-insecticides. 1699
   c) In preventive schedules, under Southern California conditions, to control Tetranychus bimaculatus on Delicious apples, 2,4-dichlorophenyl benzene sulfonate was least effective of 8 tested acaricides; for control of Paratetranychus pilosus it proved equal in control potential to 2-(p-tert-butyl phenoxy) isopropyl-2-chloroethyl sulfite, 1,1-bis-(p-chloro-phenyl) methyl carbinol, EPN, Schradan, p-chlorophenyl sulfone, being superior to p-chlorophenyl-p-chlorobenzene sulfonate, Parathion, dicyclohexylamine dinitro-o-cyclohexylphenate; in control of Bryobia praetiosa proved equal to p-chlorophenyl-p-chlorobenzene sulfonate, but inferior to dicyclohexylamine-dinitro-o-cyclohexylphenate, parathion, bis-(p-chlorophenyl) methyl carbinol, and superior to 2-(p-tert-butylphenoxy) isopropyl-2-chloroethyl sulfite, p-chlorophenyl phenyl sulfone and EPN; in control of Tetranychus bimaculatus on Bartlett pears subject to reinfestation, inferior to p-chlorophenyl-p-chlorobenzene sulfonate, 2-(p-tert-butylphenoxy) isopropyl 2-chloroethyl sulfite, p-chlorophenyl phenyl sulfone, EPN; superior only to parathion in these tests. No phytotoxicity reported in these tests. 191
   d) In greenhouse tests against Tetranychus bimaculatus on bean plants, used as a spray made from an emulsifiable concentrate, the spray containing 1 lb active ingredient per 100 gallons, 2,4-dichlorophenyl benzene sulfonate proved to have little, if any, effective residual action. 117

3) Tabular data indicating the comparative effectiveness against acarines of 2,4-dichlorophenyl benzene sulfonate may be found in the section of this work entitled Miticides or Acaricides.

4) Four grove tests of 2,4-dichlorophenyl benzene sulfonate on citrus trees under Southern California conditions to test effectiveness against Paratetranychus citri: 1698

Grove	Sprayed In	Test Interval (days)	Dosage (lbs/acre)	Av. No. Adult Mites/32 Leaf Sample		
				Wettable pwdr.	Emuls.Conc.	Comparative (Neotran®)
I Orange	April	70	2	22	5	—
"	"	70	4	10	8	2
II "	"	73	2	10	19	—
"	"	73	4	11	14	5
III "	"*	73	2	—	19	—
			4	12	14	5
			8	11	—	5
IV Lemon	July	93	6	10	—	4

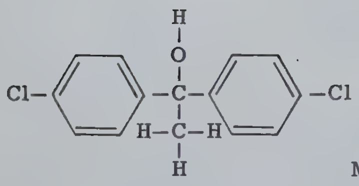
* Using a semiconcentrate at 200 gallons/acre.

5) LD_{50} (as % concentration of active ingredient) for Tetranychus telarius = 0.053%; p-chlorophenyl benzene sulfonate = 0.014% and the unsubstituted phenyl benzene sulfonate = 0.051%.

54

DI-(p-CHLOROPHENYL) METHYL CARBINOL

(Di-(p-chlorophenyl) ethanol; Bis-(p-chlorophenyl) methyl carbinol; 1,1-Bis-(p-chlorophenyl) ethanol; 4,4′-Dichloro-α-methylbenzohydrol; 4,4′-Dichloro-α-methylbenzhydrol; DMC; DCPC; Dimite®.)



Molecular weight: 367.15

GENERAL

(Also consult the general treatment in this work titled Miticides or Acaricides.)
[Refs.: 2623, 119, 1287, 117, 3150, 353, 2231, 2120, 2230, 1810, 2722, 1288, 677, 2372, 2705]

An acaricide of demonstrated value for the control of tetranychid mites of orchard trees. The toxicity of DMC for Tetranychus bimaculatus and Paratetranychus pilosus (=Metatetranychus ulmi) was recognized in greenhouse and insectary experiments in 1947. DMC is effectively toxic against the active stages of numerous mites, and lethal to their eggs. Residual action is moderate, and killing action, on the quickly paralyzed mites, is relatively slow. Insecticidal activity is relatively low, and mammalian toxicity comparatively low (approximately as toxic as DDT for laboratory animals). Precautionary labelling has been prescribed by the U. S. Department of Agriculture, Pesticides Regulation Section.

The structural relation of DMC to DDT, of which it is a somewhat distant analogue, is at once apparent. As might be expected, the technical compound contains several isomers, of which 4,4′-(p,p′-) DMC is the effective acarcide. Virtually inactive toward Paratetranychus citri.

PHYSICAL, CHEMICAL:

Colorless, crystalline solid; m.p. 69.5°-70°C; v.p. low; virtually insoluble in water; soluble in most organic solvents, notably in polar solvents, for example, in g/100 cc solvent at 25°-30°C: Toluene, 110; n-butylether, 85; ether, 152; ethanol, 125-150; tetrahydrofuran, 243; naphtha, 7; "Skellysolve B", 4.3; volatility ca 4-8 times that of DDT (2% loss in 40 days from films exposed at room temperatures); unstable toward heat and strong acids (in presence of 0.1 N sulfuric acid in alcohol, 80% dehydrated in a 5 hour refluxing; compatible with most of the commonly employed agricultural spray materials.

a) The technical product may contain, in addition to the 4,4′-(p,p′-) isomer which is the active ingredient, the following: the o,p′-, o,o′ isomers, p,p′-, o,p′-, o,o′- dichlorobenzophenone in traces, 1,1-bis-(p-chlorophenyl) ethylene and its isomers in traces. p,p′,o,p′-, o,o′-isomers of the latter substance are formed on long heating or in strongly acid media, slowly at 45°C (10% in 6 1/2 months), rapidly at 105°C (61% in 24 hours).

TOXICOLOGICAL:

1) Toxicity for laboratory animals approximately the same as that of DDT, measured as acute toxicity. 1287

2) In feeding experiments with rats the following results were obtained: 2488, 2120

1000 ppm in the diet, exposure 10 weeks: Well tolerated, slight weight loss.
2500 ppm in the diet: Produced signs of intoxication.
10,000 ppm in the diet: Quickly fatal.

a) In experiments with mice: 2488
250 mg/k in corn oil: Tolerated by oral administration.
500 mg/k in aqueous suspension, as a single oral dose: No fatalities.
> 500 mg/k in corn oil, or aqueous suspension: Brought paralysis and death.

b) In tests of the acaricidal activity of DMC on *Myocoptes musculinus* (on mice) the following results were obtained: (Mice submerged and scrubbed in the solutions 3 times at 5 day intervals.) 2993

DMC (%)	Ethanol (%)	Mice Treated	Mice Dead	Acaricidal Effect
0.4	95	10	7	100% kill.
0.4	50	36	4	100% kill.
0.2	50	44	0	100% kill.
0.1	50	14	0	A few survived.
0.05	50	14	0	A few survived.

c) An acute, oral LD_{50} for the rat of 500 mg/k is reported. The hazard for man and animals, is not serious under proper precautions. 353

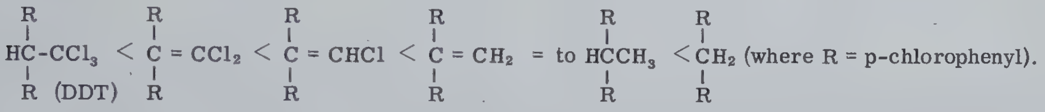
3) Phytotoxicity:

a) Employed as a 25% miscible concentrate (Dimite®) diluted 1 to 800 with water, no damage was recorded to the foliage, flowers, fruits of orchard trees or greenhouse plants. 898 353, 1698

(1) At higher concentrations, peach, grape foliage, and flowers of *Antirrhinum* and *Saint Paulia* were slightly damaged; Boston and asparagus fern may be killed by 1 to 200 dilutions of 25% concentrate. Injury to young citrus foliage has been reported.

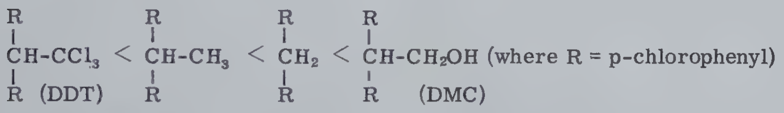
4) Toxicity for acarines:

a) General: The progressive elimination of chlorine atoms from the trichloroethane portion of the DDT molecule results in a progressive increase in acaricidal activity in the following order of rising effectiveness: 2230



$$\underset{\mathrm{R}\ (\mathrm{DDT})}{\overset{\mathrm{R}}{\mathrm{HC}}}\text{-}\mathrm{CCl_3} < \underset{\mathrm{R}}{\overset{\mathrm{R}}{\mathrm{C}}}=\mathrm{CCl_2} < \underset{\mathrm{R}}{\overset{\mathrm{R}}{\mathrm{C}}}=\mathrm{CHCl} < \underset{\mathrm{R}}{\overset{\mathrm{R}}{\mathrm{C}}}=\mathrm{CH_2} = \text{ to } \mathrm{H}\underset{\mathrm{R}}{\overset{\mathrm{R}}{\mathrm{C}}}\mathrm{CH_3} < \underset{\mathrm{R}}{\overset{\mathrm{R}}{\mathrm{CH_2}}}\ \text{(where R = p-chlorophenyl).}$$

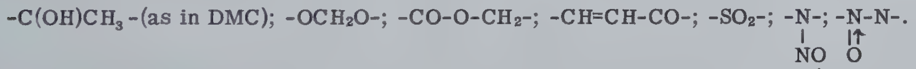
(1) The order of acaricidal activity of DDT and its remoter analogues has been given as follows: 353



$$\underset{\mathrm{R}\ (\mathrm{DDT})}{\overset{\mathrm{R}}{\mathrm{CH}}}\text{-}\mathrm{CCl_3} < \underset{\mathrm{R}}{\overset{\mathrm{R}}{\mathrm{CH}}}\text{-}\mathrm{CH_3} < \underset{\mathrm{R}}{\overset{\mathrm{R}}{\mathrm{CH_2}}} < \underset{\mathrm{R}\quad(\mathrm{DMC})}{\overset{\mathrm{R}}{\mathrm{CH}}}\text{-}\mathrm{CH_2OH}\ \text{(where R = p-chlorophenyl)}$$

(2) Although DMC [1,1-bis-(p-chlorophenyl] ethanol) is highly acaricidal, 1,1-bis (p-chlorophenyl) methanol is almost inactive. 353

(3) Apparently, acaricidal activity is associated with molecules having two benzene nuclei bridged by certain groups. Toxicity is modified by altering the bridging group and substitution in the benzene nuclei. Chlorine in the para position is associated with maximum acaricidal activity. The most effective bridging groups appear to be: 898



$$\text{-C(OH)CH}_3\text{-(as in DMC); -OCH}_2\text{O-; -CO-O-CH}_2\text{-; -CH=CH-CO-; -SO}_2\text{-; }-\underset{\mathrm{NO}}{\mathrm{N}}-;\ -\underset{\underset{\mathrm{O}}{\uparrow}}{\mathrm{N}}-\mathrm{N}-.$$

(4) o,p′-, o,o′-isomers of DMC are much less effective acaricides than the p,p′ isomer. Activity retained if the α-methyl is replaced by ethyl, cyclohexyl; lost if replaced by phenyl, benzyl. Shift of alcohol group to tertiary C atom to give 2,2-bis(p-chlorophenyl) ethanol brings loss of activity. 1287

b) Relative toxicity of DMC and other DDT-related acaricides for *Paratetranychus citri* and *Tetranychus bimaculatus*: 2230

Compound	LC_{50} 24 hr (%) For *Paratetranychus citri*	LC_{50} 24 hr (%) For *Tetranychus bimaculatus*	
1,1-Bis-(p-chlorophenyl) ethanol (DMC)	0.1	0.035	
Bis-(p-chlorophenoxy) methane	0.025	<1.0	*
Bis-(p-chlorophenyl) methane	0.25	0.25	
2-(p-Chlorophenyl)-1,1,1-trichloroethanol	0.2	0.4	
p-Chlorobenzyl-p-chlorophenyl ether	0.13	—	
Di-(p-chlorophenyl) ether	1.0 (LC_{57})	—	
p-Chlorophenyl-p-chlorobenzoate	1.0	—	
Bis-(p-methylphenoxy) methane	0.09	—	
DDT	non-toxic at 10%	—	

* 1% residues on oranges still lethal after 2 month outdoor exposure.

c) LC_{50}, LC_{90} values of DMC and other acarcides for the green and red forms of *Tetranychus bimaculatus* on bean leaves; Comparative toxicity: 565

Compound	Method	Time of Mortality Count Hrs.	LC_{50} (ppm) Red Form	LC_{50} (ppm) Green Form	LC_{90} (ppm) Red Form	LC_{90} (ppm) Green Form
DMC	Dip	24	9.6	6.8	26.5	20
"	Dip	48	8	6	28.5	19
"	Dip	72	7.9	4	17.5	12
"	Spray	48	31	26	78	60

c) LC_{50}, LC_{90} values of DMC and other acaricides for the green and red forms of Tetranychus bimaculatus on bean leaves; Comparative toxicity: 565

Compound	Method	Time of Mortality Count (Hrs.)	LC_{50} (ppm)		LC_{90} (ppm)	
			Red Form	Green Form	Red Form	Green Form
Aramite®	Dip	48	2.9	2.9	18	19.5
"	Spray	48	22	14	93	72
TEPP	Dip	24	3.8	2.5	13.0	17.0
EPN	Dip	24	5.5*	3.9*	20.0	12.0
Malathion	Dip	48	36**	48**	96	120

* = Significant difference at 5% level; ** at 2% level.

d) Comparative toxicity, DMC and other compounds. Topical application to ♀ Tetranychus bimaculatus: 1121

Compound	LD_{50}		LD_{100}	
	μg/mite	mg/k	μg/mite	mg/k
DMC	4.2	210	8.0	400
Etoxinol	3	150	7.8	390
Chlorobenzilate	2	100	3	150
Pyrazothion	1.2	60	2.2	120
Pyrazoxon	0.1	5	0.76	3.8
Diazinon	0.2	100	4.4	240
Parathion	1.8	90	4	200
Systox	0.4	20	0.76	38

e) Comparative toxicity DMC and other compounds to Tetranychus bimaculatus. Emulsifiable concentrates applied to mites on bean leaves by settling tower method: 905

Compound	LC_{50} 2 days after treatment (g/100cc)			
	Adult	Larva	Egg	Adult*
DMC	0.044	0.042	0.082	0.21
Aramite®	0.0038	.0072	.174	.041
Chlorobenzilate	.012	.014	.078	.12
Bis-(p-chlorophenyl) ethinyl carbinol	.03	.033	.079	.48
Ovotran®	.45	.019	.076	5.0 +
p-Chlorophenyl pheny sulfone	.21	.23	.35	4.6
2,4-Dichlorophenyl benzene sulfonate	0.78	.21	.39	5.0 +
Parathion	.0056	.013	.19	.021
Malathion	.0025	.0073	.32	.084
EPN	.0025	.0047	.23	.042
Demeton	.0022	.0028	.097	.003

* Adult mites on leaf surface opposite the treated surface.

f) Comparative residual activity DMC and other compounds for Tetranychus bimaculatus. Greenhouse tests on bean plants: 117

Compound	Lb/100 gal Active Ingredient	% Mortality At Stated Period Between Spraying And Infesting				
		1 day	3 days	7 days	10 days	14 days
DMC	0.25	99.9	100	86.0	99.5	89.4
EPN	0.079	100	100	99.7	100	80.0
p-Chlorophenyl-p-chlorobenzene sulfonate	1.0	90.3	75.6	82.8	91.4	80.3
DNOCHP	0.31	100	94.8	80.0	99.6	61.0
"	.16	72.6	70.2	32.0	23.4	10.7
Neotran®	1.0	86.9	85.4	93.3	55.0	15.7
88R	0.188	98.3	97.4	72.0	47.0	17.3
Parathion	0.3	99.8	94.4	54.3	51.6	19.5
Arathane	0.5	90.2	84.8	24.0	34.3	52.1
IN-4200	0.75	85.4	91.0	26.9	18.7	8.4
DNOCHP, NH_4 salt	0.31	92.6	70.1	33.0	37.9	19.8
" " "	0.16	26.7	25.2	16.3	13.9	14.5
DNOCHP, Monoethanolamine salt	0.31	89.6	69.8	40.0	26.0	14.5
" " "	0.16	21.2	11.6	10.3	6.1	8.3
2,4-Dichlorophenyl benzene sulfonate	1.0	46.8	41.6	12.1	32.6	27.6

g) Residual toxicity of DMC for Tetranychus bimaculatus, in greenhouse tests on Phaseolus coccineus plants, used as a 50% wettable powder at 0.5 lb/100 gallons. Over 1000 mites examined in each case: 117

Days Between Spraying And Infestation	% Mortality After	
	7 days	14 days
1	97.2	99.9
2	98.1	100
3	96.4	100

g) Residual toxicity of DMC for Tetranychus bimaculatus, in greenhouse tests on Phaseolus coccineus plants, used as a 50% wettable powder at 0.5 lb/100 gallons. Over 1000 mites examined in each case: 117

Days Between Spraying And Infesting	% Mortality After	
	7 days	14 days
4	92.7	99.6
5	93.7	99.7
6	95.1	96.2
7	94.1	86.0
10	98.2	99.5
14	89.0	89.4
Control	3.0	3.6

h) Field tests of DMC in the control of Paratetranychus citri in 7 citrus groves under Southern California conditions; used as a spray at 1600 gals/acre: 1698

Grove		Sprayed In	Test Interval (days)	Dosage (Lbs/acre)	Av. No. Adult Mites/32 Leaf Sample	
					DMC Treated	Neotran® Treated
I	(orange)	March	15	4 (as dust)	20	13
II	(lemon)	September	34	16	20	17
III	(orange)	March	41	4	15	3
"	"	"	"	8	8	1
IV	(orange)	April	73	6	6	6
V	(orange)	July	77	4	22	—
VI	(orange)	December	126	4	9	6
VII	(lemon)	January	131	8	17	5

(1) Less effective than Neotran® at same dosages in 7 groves.

(2) Injury to young foliage where 8-16 lbs/acre were used in relatively warm weather.

i) Comparative toxicity of DMC and other compounds to a non-resistant® and an acaricide— resistant strain in Tetranychus bimaculatus. Acaricides used as Methyl chloride aerosols in greenhouse tests: 2867

Acaricide	% Mortality	
	Non-R Mites	R-Mites
DMC	97	22
Aramite	100	2
Sulfotepp	100	59
TEPP	97	12
HETP	99.7	39
Methyl parathion	100	1
Para-oxon	100	6
Parathion	99.9	5
Tetraisopropyl pyrophosphate	98	38

j) Other comments on comparative toxicity of DMC and other compounds in field tests for the control of various acarines:

(1) Used as a 25% concentrate at 1.5 pints/100 gallons, DMC is reported to have had a longer residual effect than any non-systemic acaricide against Tetranychus bimaculatus, T. pacificus, Bryobia praetiosa, Metatetranychus ulmi, Eotetranychus carpini borealis in apple orchards of the Pacific Northwest. 1 application in June usually gave season-long control. 727

(2) Vs. Paratetranychus pratensis: Erratic results in control of, on wheat in New Mexico where best control was given by Systox, parathion. Less than 75% control with DMC. 1442

(3) Petrobia latens on dryland wheat: At 0.25-0.5 lb/acre DMC gave control equal to that given by TEPP (0.25-.5 lb/acre), EPN (0.5 lb/acre), Malathion (0.75 lb/acre), R-242 (1.0-2.0 lbs/acre), toxaphene (3.0 lbs/acre), Compound 876 (0.5 lb/acre), endrin (0.15-0.3 lb/acre). Superior to BHC at 0.5-1.0 lb/acre, but inferior to Demeton (.5 lb/acre) parathion (0.5 lb/acre), demeton (0.25 lb/acre), parathion (0.25 lb/acre), metacide (0.25-.5 lb/acre) Schradan (0.5 lb/acre), NPD (0.5-1.0 lb/acre) chlorobenzilate (0.5 lb/acre) Aramite® (0.33-0.66 lb/acre), Ovotran® (0.5-1.0 lb/acre) compound 923 (1.0-2.0 lbs/acre). Tests based on counts made 5 days and 2 weeks after treatment.

(4) Vs. Metatetranychus ulmi: 100% kills of adults and summer eggs were reported. Increasingly 900, 119
poor control demonstrated in British Columbia using DMC. As an emulsion, failed to control (England) 2203
in field trials, although toxic in the same formulation to summer eggs in laboratory trials. 1808, 1810

(5) Vs. Paratetranychus citri: Nearly inactive to adults of. 1810

(6) Tetranychus bimaculatus: In control of, by preventive schedules on apple trees, Southern California, 191
DMC proved equal to Schradan, 2(p-tert-butylphenoxy) isopropyl-2-chloroethyl sulfite, and superior to Ovotran®, Sulfenone®, EPN, parathion, DN-111, Genite®.

Paratetranychus pilosus: In control of, under the conditions given above proved equal to all the compounds mentioned save to DN-111, to which DMC and the others were superior.

Bryobia praetiosa: In control of, under the conditions given above, DMC proved equal to DN-111, parathion, and superior to all others tested.

5) Miscellaneous comments on toxicity; acarines:
  a) The unsubstituted analogue, Diphenyl carbinol (Benzohydrol), is of low activity for eggs and adults of *Metatetranychus ulmi*, and the eggs of *Tetranychus telarius*. 900, 2587
  b) The n-butyl analogue, di-(p-chlorophenyl)-n-butyl carbinol, is inactive for the eggs of *Tetranychus telarius*.

6) Pharmacological, pharmacodynamical, physiological; Acarina:
  a) DMC exercises a slow killing action on the active stages of many mites, producing a semi-paralysis from which the mites may be aroused to violent convulsion in response to stimuli. The suggestion of a DDT-like neurotoxic action is evident. 2231
  b) DMC evidences a synergistic action with DDT when both are used in combination as residues to control DDT-R strains of *Musca domestica*. 3009 3011
    (1) 1 part DMC to 100 parts DDT showed marked activity against DDT-R flies.
    (2) Activity becomes optimal at 1 part DMC to 10 parts DDT, and declines sharply at a proportion of 10 parts DMC to 1 part DDT.
    (3) When DMC was used as 0.1-0.3% the amount of DDT a mortality of more than 71% was obtained among DDT-R flies. 2936
    (4) There is evidence that DMC blocks the mechanism of DDT detoxification in resistant (DDT-R) *Musca domestica*. 2473
    (5) Effect of DMC on the inhibition of the conversion of DDT to DDE 24 hours after application to DDT-R *Musca*: 2473

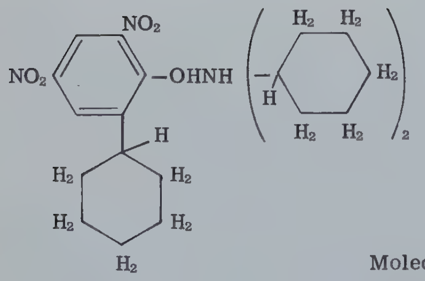
Applied (µg/fly)		Recovered Internally As % DDT Applied		% Inhibition	% Mortality
DDT	DMC	DDT	DDE		
0.65	0	0	78.4	—	0
0.65	0.06	9.4	63.0	19.6	2.0
0.65	.13	16.9	58.4	25.5	14.0
0.65	.32	27.7	49.2	37.2	25.0
0.65	.65	44.6	40.0	49.0	50.0
0.65	1.30	53.8	27.7	64.7	72.0
0.65	3.25	69.2	18.4	76.5	92.0
0.65	6.50	76.9	12.3	84.3	100

  c) The parathion-R strain of *Tetranychus telarius* is not significantly resistant to DMC. 2354

7) For screening test data: DMC vs. lice, mosquito larvae, chiggers, flies see Ref. 1801.

55

DICYCLOHEXYLAMMONIUM 4,6-DINITRO-o-CYCLOHEXYLPHENATE (DN-III; Dicyclohexylamine salt of 4,6-dinitro-o-cyclohexylphenol; Dicyclohexylamine salt of DNOCHP; Dynone II.)



Molecular weight: 447.56

GENERAL

(Also consult in this work the section titled Dinitrophenols)
[Refs.: 353, 2231, 2120, 1744, 120]

A selective acaricide and ovicide; effective against some mites, thrips, scale insects. In this salt the phytotoxic properties of 4,6-dinitro-o-cyclohexylphenol are markedly reduced without serious reduction of acaricidal or insecticidal activity. Effective, according to reports, on peach trees, but erratic in results on apple trees.

PHYSICAL, CHEMICAL:

Orange-colored, crystalline solid; m.p. ca 197°C; decomposes on heating to 204°C; less volatile (lower v.p.) than

4,6-dinitro-o-cyclohexylphenol; virtually insoluble in water (0.0037 g/100 g H_2O at 20°C), soluble in some organic solvents, for example, g/100 g solvent: at 25°C ethanol 1.76; appreciably soluble in acetone, alcohol, benzene, slightly soluble in petroleum oils; readily hydrolyzes, yielding dinitro-o-cyclohexylphenol which is susceptible, in its turn, to further reduction. Formulated: As a 20% wettable powder; as a dust (1.7%) on Frianite, a volcanic earth.

TOXICOLOGICAL:

1) Acute toxicity for higher animals:
   a) Very toxic to man and animals, particularly if ingested.

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	ca 330		1951
Rat	or	LD_{50}	400		2935
Rat	or	LD_{100}	600		2935
Guinea Pig	ct	LD_{100}	> 1000	Single, acute application.	2935

2) Chronic toxicity for higher animals:
   a) Rabbits, receiving in the diet 500 and 1000 ppm, showed losses in weight which were not deemed significant. 2935
   b) Rabbits, receiving 2000 ppm in the diet, showed losses in weight of 15%. Cloudy swelling of slight degree was present in the liver tissues. 2935

3) Phytotoxicity:
   a) Because of the presence of free phenolic groups, the dinitrophenols have a high phytotoxic potential. 2120
   b) The dicyclohexylamine salt reduces the vapor concentration of the parent compound, 2,4-dinitro-6-cyclohexylphenol, q.v. In so doing the phytotoxicity is lowered, and the insecticidal and acaricidal action is almost wholly retained. 2120 2231

4) Toxicity for insects and acarines:
   a) It may be noted here that the ethanolamine (monoethanolamine), triethanolamine salts, of DNOCHP are also effective acaricides and insecticides. 2358 353
   b) Toxicity of DN-111 for Apis mellifera: 927

Route	Concentration	% Mortality At		
		24 hrs	48 hrs	72 hrs
or	1:800 in Honey-H_2O 1:1	80	95	100
or	1:1600 in Honey-H_2O 3:1	45	45	50 (all "sick")
or	1:1600 in Honey-H_2O 3:1	35	35	35 (all "sick")
Contact Spray	1:400 Suspension in H_2O at ca.005 g/cm²	0	5	5
Contact Spray	10% In Acetone at .004 g/cm²	50	60	60
Contact Spray	1:400 Suspension in H_2O	0	0	0 ("affected")
Contact, Deposits	0.0004 g/cm² (5 days exposure on card)*	100	—	—
Contact, Deposits	0.0004 g/cm² (6 days exposure on card)*	80	100	—
Contact, Deposits	0.0004 g/cm² (16 days exposure on card)*	40	40	60

*Exposure of DN-111 deposits prior to exposure of insects.
Direct contact, dusts 10% at 400 mg/cage, vacuum dusting; mortality: 2 hr-91%, 4 hr-97%, 6 hr-100%. 131

   c) Tetranychus telarius, control of: DN-111 gave 98% control, in contrast to 66% control with lime-sulfur, 27% control with elemental sulfur; by comparison, the NH_4 salt of dinitro-o-cresol killed foliage before killing mites. For Tetranychus pacificus the monoethanolamine salt was more effective. 2843 353
   d) Paratetranychus ununguis, control of: 0.01% solutions yielded 99% control of the spruce mite. 2358
   e) Residual toxicity of the related NH_4 and monoethanolamine salts of DNOCHP for Tetranychus bimaculatus; greenhouse tests on bean plants: 117

Compound	Active Ingredient (lb/100 gal)	% Mortality At Stated Period Between Spraying And Infesting				
		1 day	3 days	7 days	10 days	14 days
DNOCHP, NH_4 salt,	0.31	92.6	70.1	33.0	37.9	19.8
DNOCHP, NH_4 salt,	0.16	26.7	25.2	16.3	13.9	14.5
DNOCHP, monoethanolamine salt,	0.31	89.6	69.8	40.0	26.0	14.5
DNOCHP, monoethanolamine salt	0.16	21.2	11.6	10.3	6.1	8.3
DNOCHP (for comparison)	0.31	100	94.8	80.0	99.6	61.0
DNOCHP (for comparison)	0.16	72.6	70.2	32.0	23.4	10.7
Dinitro-caprylphenyl crotonate*	0.5	90.2	84.8	24.0	34.3	52.1
DMC (for comparison)	0.25	99.9	100	86.0	99.5	89.4
EPN (for comparison)	0.079	100	100	99.7	100	80.0
Parathion (for comparison)	0.3	99.8	94.4	54.3	51.6	19.5

* = Arathane®, for comparison.

   f) Tested in preventive spraying schedules in apple orchards (Delicious) under Southern California conditions: 191
      (1) Substances tested: Dicyclohexylamine salt of DNOCHP (A) and the following:

1,1-Bis-(p-chlorophenyl) methyl carbinol (B)
2-(p-tert-Butylphenoxy) isopropyl-2-chloroethyl sulfite (C)
Octamethyl pyrophosphoramide (D)
p-Chlorophenyl-p-chlorobenzene sulfonate (E)
p-Chlorophenyl phenyl sulfone (F)
Ethyl-p-nitrophenyl thiono-benzene phosphonate (G)
Parathion (H)
2,4-Dichlorophenyl benzene sulfonate. (I)

(2) In control of Tetranychus bimaculatus: All superior to (A) save (I) which was inferior.
In control of Paratetranychus pilosus: All superior to (A).
In control of Bryobia praetiosa: (A) = (H) = (B) and superior to the others.

(3) No phytotoxic damage reported for (A).

g) Tested in the field (citrus orchards), against Aceria sheldoni DN-111, employed as a wettable powder in preliminary trials, failed to control. The failure was shared by numerous other toxicants. 1699

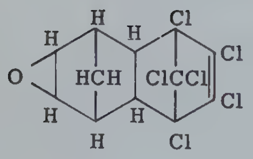
h) Tested against Tetranychus bimaculatus on bean leaves, sprayed in a settling tower (method of Ebeling and Pence) the mites being placed on the sprayed leaves after treatment, the following results were obtained: 905

	LC$_{50}$ (g/100cc) 2 days post-treatment			
	Adult	Larva	Egg	Adult On Surface Opposite Treated Surface
DN-111	0.082	0.031	0.28	1.44 Wettable powder.
Aramite®	.0038	.0072	.174	.041 Emulsifiable conc.
EPN	.0025	.0047	.23	.042 " "
Demeton	.0022	.0028	.097	.003 " "
DN-289	.0083	.0072	.038	.24 " "

5) For pharmacological, pharmacodynamical, physiological, etc., considerations consult the general treatment on Dinitrophenols in this work.

56

DIELDRIN (1, 2, 3, 4, 10, 10-Hexachloro-6, 7-epoxy-1, 4, 4a, 5, 6, 7, 8, 8a-octahydro-1,4-endo, exo-5,8-dimethanonaphthalene; 1, 2, 3, 4, 10, 10-Hexachloro-6, 7-epoxy-1, 4, 4a, 5, 6, 7, 8, 8a-octahydro-1,4, 5, 8-dimethanonaphthalene; Hexachloro-epoxy-octahydro-dimethanonaphthalene; HEOD; Compound 497; Octalox; 1:2:3:4:11:11: Hexachloro-6:7-epoxy-1:4:5:6:7:8:9:10-octahydro-1:4:5:8-diendomethylene naphthalene.)



Molecular weight 381 (380.926)

GENERAL

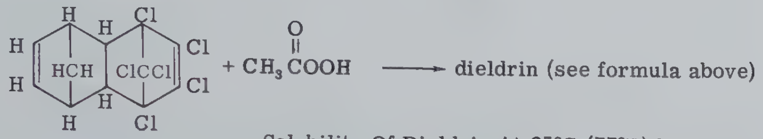
[Refs.: 353, 2231, 2120, 2812, 129, 89, 3199]

One of the cyclodiene group of insecticides comprising dieldrin, chlordane, heptachlor, aldrin, isodrin, endrin, toxaphene, q.v. These are all highly chlorinated, cyclic hydrocarbons. Also considered to be chlorinated terpenes. Characteristic is the endomethylene bridged structure. Save for toxaphene, these insecticides are made by the Diels-Alder diene reaction. The range of insecticidal activity, and usefulness, is exceptionally wide. Possesses a pronounced residual action, comparable to that of DDT, and is useful in the control of many forms for which DDT is either unsuccessful or only partly effective. Extensive use in control of household and agricultural insects, grasshoppers, locusts, crickets, cotton insects, soil inhabiting insects.

In the U. S., the term dieldrin signifies the presence of not less than 85% of the compound named above, and not more than 15% of related, insecticidally active compounds. Dieldrin is considered a general poison. It has toxic activity both as a stomach and contact poison. At dosages considerably greater than those insecticidally employed, dieldrin seems to be free of adverse effect upon plants.

PHYSICAL, CHEMICAL

The pure substance (recrystallized, 99% pure) is a white, crystalline solid; technical, a light, tan, flaky solid with a mild, chemical odor; water content $<0.1\%$; free acid, $<0.4\%$ (calculated as acetic acid); insoluble residue (xylene), $<0.5\%$; m.p. 176-177°C; $d_{4^\circ}^{20^\circ}$ 1.75 (lbs/gallon at 68°F = 14.1); v.p. 1.8×10^{-7} mm Hg at 25°C (77°F); setting point (minimum) 203°F; bulk density 47-51 lbs/ft^3; less volatile than DDT at $>$ 43°C; Insect: more volatile at $<$ 43°C; not flammable; stable in alkalis, dilute acids, and toward light; reacts with strong acids, acid catalysts, oxidants, phenols, and active metals; forms the halohydrin on refluxing in halogen acids; not corrosive at room temperatures; compatible with other insecticides and fungicides in current use; 8 steric isomers of the compound are possible. The residual action exceeds that of aldrin, the volatility of dieldrin being 1/30th that of aldrin. Dieldrin is the epoxide of aldrin, formed by the action on aldrin of peracetic or perbenzoic acid:



Solvent	Solubility Of Dieldrin At 25°C (77°F) In Representative Solvents:		
	At Saturation (% w)	G/100 cc Solvent	G In 100 cc Of Solution
Acetone	25	26	22
Amyl acetate	28	32	27
Benzene	39	56	40
n-Butanol	7	5	5
Carbon tetrachloride	24	48	38
Deobase oil	9	4	4
Dipentene	21	22	20
Ethanol	5	4	4
Ethylene dichloride	36	70	48
Fuel oil	17	17	15
Isopropyl alcohol	4	2	2
Deodorized kerosene	6	5	5
Methanol	1	1	1
Methyl cellosolve	11	12	12
Methyl ethyl ketone	33	39	32
Pentane	4	2	2
Sovacide 544-C	28	37	30
Summer diesel fuel	17	17	15
Toluene	39	54	41
Turpentine	17	17	15
Winter diesel fuel	7	6	6
Xylene	37	52	38
Water	$<$ 0.1 ppm	—	—

Formulations: Emulsifiable concentrate (1.5 lbs dieldrin/gallon) recommended in control of boll weevil, southern green stink bug, rapid plant bug, cotton fleahopper, grasshoppers, thrips, tarnished plant bug, fall army worm, certain cut worms, Say's plant bug, brown cotton bug (on cotton for early season control at rate of 0.05 lb dieldrin/acre, mid-season control 0.10 lb/acre, late season control 0.15 lb/acre save for boll weevil for which 0.15 lb/acre for early, 0.15-0.4 lb/acre for mid, late season control; cutworms: 0.1 lb/acre for early season control.

50% wettable powder (0.5 lb dieldrin/lb) recommended for fruit insects, for example, plum curculio of apples, apricots, cherries, peaches, plums, prunes, Lygus and stink bugs of peaches.

1.5% dusts recommended at 5-10 lbs/acre for early season, 10-15 lbs/acre for late season control of boll weevil, southern green stink bug, rapid plant bug, cotton fleahopper, grasshoppers, thrips, tarnished plant bug, fall army worm, cutworms (some), Say's plant bug, brown cotton bug.

0.5% solutions for household insects, for example, roaches, silver fish, ants, carpet beetles and others such as paper and mud-dauber wasps, brown dog tick.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	40-50	Roughly 5 times as toxic as DDT.	89
Rat	or	LD_{50}	100		1950
Rat	or	LD_{50}	65		2547
Rat	or	LD_{50}	50-75	Intoxication symptoms may be several days delayed.	1950
Rat ♀ (25-31 days)	or	LD_{50}	38.3(32.7-44.8)	0.1-2% sol in peanut oil, death within 14 days.	3128, 3121

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat ♀ (170-220)	or	LD_{50}	34		3121
Rat ♂	or	LD_{50}	47		3128
Rat	or	LD_{50} ca	87		1951
Rat	or	LD_{50}	50-55		1988
Rat ♀	ct	LD_{50}	60	In xylene, roughly 40 times as toxic as DDT.	89
Rat ♂	ct	LD_{50}	90	In xylene, roughly 40 times as toxic as DDT.	89
Rabbit	ct	LD_{50}	150	As a 4% solution of dieldrin, technical.	1952
Rabbit	ct	MLD	250-360	Single dose, dry, skin contact 24 hrs under rubber sleeve.*	3121, 3124
Rabbit	ct	MLD	360-600	10% w/v olive oil dispersion, 24 hr contact, rubber sleeve.*	3124
Rabbit	ct	MLD	40-163	Dry** Skin contact (unabraded, intact skin) 2 hrs/day, 5 days/week for 10 weeks. 50 applications.	3121, 3124
Rabbit	ct	MLD	19-50	In peanut oil***	3121, 3124
Rabbit	ct	MLD	< 5.3	In ultrasene****	3121, 3124
Dog	or	LD_{50}	65-95	As a single acute dose.	2548
Sheep	or	LD_{50} ca	50	Intoxication symptoms may be several days delayed.	1950
Pig	or	LD_{50} ca	50	Intoxication symptoms may be several days delayed.	1950
Chicken (7 days old)	or	LD_{50}	43	Tech. dieldrin; death in 1/2 - 5 days, older birds less susceptible. In acetone.	2824
Chicken (3-6 weeks old)	or	LD_{50}	20-30		922
Fish (All those tested)	Medium	LC	0.125 ppm	Extremely hazardous.	1507

* Tremors, convulsions, observed often; mild skin erythema noted rarely, the skin usually remaining normal, unchanged.

** Repeated contact with dry, powdered dieldrin brought about no gross changes in skin.

*** Slight irritation, scaliness, of exposed skin.

**** Fissuring, ulceration, hemorrhage, of exposed skin. Ultrasene alone induced similar effects.

a) Dermal toxicity of dieldrin to the albino rat; absorption by the unabraded, intact skin: 1454

Formulation	Single Dosage mg/k	Doses (No.)	Mortality No. Dead/No. Tested	Mortality %
Technical powder, dry*	400	1	20/20	100
Technical powder, dry*	100	1	7/10	70
Concentrate, 25%	400	1	42/43	97
Solution, 6.25%	100	1	17/25	68
Emulsion, 2.5%	40	< 16	76/90	84
Emulsion, 1.25%	20	> 100	9/20	45
Emulsion, 0.62%	10	> 100	10/30	30

* Note that dry, powdered, technical dieldrin is absorbed by the intact skin virtually as readily as are solutions of dieldrin in organic solvents.

(1) On basis of experiments with rats, mice, hamsters, Guinea pigs, rabbits, dogs, cats, monkeys, it is suggested that a single skin contamination of 100 cc or more, 25% dieldrin solution may be dangerous to a human being unless promptly washed away. 1454

(2) The acute oral toxicity of dieldrin for mammals may be considered relatively low when compared with the high dermal toxicity. 1454

b) Comparative toxicity of dieldrin, and closely related substances, for higher animals:

Substance	Animal	Route	Dose	Dosage (mg/k)	Remarks	
Aldrin	Rat	or	LD_{50}	45.9 (35.8-54.2)	Solutions in peanut oil, 0%-2%	3128
Dieldrin				38.3 (32.7-44.8)		
Isodrin				16.4 (12.6-21.5)		
Endrin				16.8 (13.0-21.7)		
Aldrin	Chicken (7 days old)	or	LD_{50}	25.5	Solutions in acetone administered in capsules.	2824
Dieldrin				43.0		
Isodrin				2.7		
Endrin				3.5		
DDT	Rabbit ♀	ct (single dose)	MLD	> 2500	As single applications of dry, recrystallized powder 24 hr skin contact under rubber sleeve.	3128
Aldrin				600-1250		
Dieldrin				250-360		
Isodrin				< 94		
Endrin				60-94		

Substance	Animal	Route	Dose	Dry	In Oil	In Ultrasene	
DDT	Rabbit ♀	ct (multiple dose)	MLD	213-489	109-257	> 46	Exposures of 2 hrs/day, 5 days/week for 10 weeks.
Aldrin				35-123	10-26	< 4.8	
Dieldrin				40-163	19-50	< 5.3	
Endrin				< 30			

b) Comparative toxicity of dieldrin, and closely related substances, for higher animals:

Substance	Animal	Route	Dose	Dosage (mg/k)		
Chlordane (tech)	Rat	or	LD_{50}	457-590	Values from various sources quoted by →	2231
α-Chlordane				700		
Heptachlor				90		
Aldrin				67		
Dieldrin				87		
Isodrin				12-17		
Endrin				10-12		
Toxaphene				69		
Strobane ®				200		

Substance	Animal	Route	Dose	Single Application (dry)	Repeated Application Daily		
Chlordane	Rabbit	ct	LD_{50}	< 780	20-40	Various sources quoted by →	2231
Heptachlor				2000	< 20		
Aldrin				< 150	< 5		
Dieldrin				< 150	< 5		
Toxaphene				> 4000	40		

2) Chronic toxicity for higher animals:

a) Dieldrin may be absorbed by the animal body via mouth, intact skin, inhalation. The greatest hazard is that of skin absorption. 89

b) Reported that no observable chronic injury has been shown by human workers engaged in the manufacture of dieldrin. The formulation and application hazard probably exceeds the manufacture hazard. 2548

c) Approximate toxicity (DDT = 1): acute oral 3, chronic oral 4-100, dermal (single exposure) 30, multiple exposure 30.

d) Dieldrin as a spray for livestock:

(1) Not too safe for repeated use. 0.25% concentrations have been toxic to week old calves; 2.0% concentrations toxic to cattle; 3.0% concentrations toxic to sheep, goats. Hogs tolerated concentrations of ca 4.0%. Harmless to calves at 0.1% as emulsion sprays. 2571, 1636

(2) Cattle, sprayed 3 times at 2 week intervals with 0.5% concentrations, showed clinical signs of intoxication.

(3) Dieldrin is stored in, and long retained by, the fat of domestic animals and secreted in the milk of exposed, lactating animals. Yearling cattle, receiving 25 ppm in diet, showed 75 ppm in fat on 28th day, 74 ppm on the 56th day; sheep, on diets with 25 ppm, showed 43 ppm in fat on 28th day, 69 ppm after 56 th day; detectable amounts still present 32 weeks after cessation of feeding.

e) Dieldrin as an animal dip:

(1) Rabbits, immersed for 2 minutes in wettable powder formulations at concentrations equivalent to 400-500 mg/k, showed symptoms of intoxication: Loss of appetite, extreme nervousness, convulsions, wild running, falling, kicking, with muscular spasms of 3-10 minutes duration. Similar symptoms followed treatment with aldrin at 15-25 mg/k, toxaphene at 1025-1075 mg/k. 1713

(2) Rats are said to have survived dips of concentration equivalent to 2000-3500 mg/k. As in rabbits, the chronic symptoms in rats are loss of appetite and weight, convulsions. 1636

f) Experiments on the cumulative dermal toxicity of dieldrin applied dry; in olive oil; in Ultrasene: 3124, 3128

(1) Rabbits (3), in daily contact with dry dieldrin, 2 hrs/day: 5 days/week: 10 weeks, at 100 mg/animal/day (av. of 40 mg/k) survived 50 contact periods; at 300 mg/animal (av. 163 mg/k) 4/5 animals died after 9, 11, 15, 21 contact periods. (600 mg/animal of DDT, dry, survived.)

(2) Rabbits (3), receiving 50 mg/animal (av. 19 mg/k) in peanut oil 2 hrs/day: 5 days/week: 10 weeks, survived 50 contact periods; death for all at doses of 100 mg/animal (av. 50 mg/k); died after 8, 10, 12 contact periods. (300 mg/animal DDT in olive oil, tolerated.)

(3) Daily dose of 12 mg/animal in Ultrasene, 2 hrs/day: 5 days/week fatal to 2/3 after 17, 34 contact periods; 1 survived 50 contact periods. (2/3 survived 50 contacts of DDT in Ultrasene at 100 mg/animal; 1 death after 21 contacts.)

(4) Survivors of contact with dry dieldrin showed slight growth rate retardation; survivors of dieldrin in peanut oil, Ultrasene, (contact) showed moderate growth retardation; animals dead from any type of contact application showed loss of weight before death.

(5) Experiments with rats, mice, hamsters, guinea pigs, rabbits, dogs, cats, monkeys, suggest that a single skin contamination of 100 cc or more of 25% dieldrin solution may be dangerous to man unless promptly washed away. However, minor daily skin contaminations with ordinarily employed field spraying concentrations, on the basis of the following tests, may be tolerated without appreciable damage. Technical powder is absorbed almost, or quite as, readily by the unbroken skin as dieldrin dissolved in organic solvents. Immediate washing was of some (but not enough) benefit to protect all subjects from even a single application of a 25% dieldrin concentrate or from repeated applications of a 2.5% emulsion. Delayed washing is of no benefit. 1454

Mortality of Albino Rats receiving dermal applications of dieldrin formulations:

Formulation	Single Dosage (mg/k)	No. of Doses	Mortality Fraction	Mortality %
Technical powder	400	1	20/20	100
Technical powder	100	1	7/10	70
25% Concentrate	400	1	42/43	97
6.25% Solution	100	1	17/25	68
2.5% Emulsion	40	< 16	76/90	84
1.25% Emulsion	20	> 100	9/20	45
0.62% Emulsion	10	> 100	10/30	30
Control	0	> 50	2/10	20

(a) Dieldrin poisoned animals showed convulsions, appetite loss, weight loss, and various pre- and post-convulsive disorders. In acute poisoning, convulsions may bring rapid death before much weight is lost. However, weight loss was the most nearly common sign of dieldrin poisoning in various animal species. Weight loss may precede or follow convulsions if these develop, and is due directly to starvation and not to increased metabolic rate, greatly disturbed fluid balance or other disorder. A dieldrin treated rat undergoes marked "voluntary" starvation and reduced water intake as soon as application of a significant amount of dieldrin begins, yet the weight loss is no greater than that of an untreated animal forcibly starved to the same degree.

(b) Pre- and post- convulsive disturbances included: Hyperexcitability, failure of co-ordination, choreiform motions, weakness, excess salivation, blepharospasm, jaw-champing, twitching of isolated muscle groups, "personality" changes.

(c) Convulsions, while chiefly clonic, may end in a tonic phase with complete limb and body extension. A convulsion is followed at once by coma, after which recovery may ensue. Convulsions ordinarily lasted ca 1 or 2 minutes, but may be prolonged to 30 minutes. The coma was brief, but in animals which have suffered several seizures the post-convulsive coma progressively lengthens to become, eventually, continuous. Of the various signs of poisoning only long-continued coma and weight loss are apparently mortal.

(d) Autopsy of dieldrin-killed animals revealed no specific lesions, per se, sufficient to account for death.

(e) Barbiturates, as antidotes, have yielded encouraging results in dogs, and monkeys brought to severe convulsion by dieldrin. Rats, hamsters, rabbits, cats, fail to respond, but the life of barbiturate treated cats is prolonged. In dogs, monkeys, barbiturate sedatives reduce, but do not at once eliminate, hyperexcitability, incoordination, convulsions. Sedatives affect the appetite directly permitting dieldrin intoxicated subjects to improve their nutritional state.

g) Prolonged (2 year) feeding experiments with rats: 3125, 3128

(1) On diets containing 2.5, 12.5, 25.0 ppm dieldrin, ♂, ♀ rats showed average weight gains = to or > than controls; no significant increase in mortality over controls.

(2) After 18 months to 2 years, ♂, ♀ rats, on 2.5 ppm dieldrin, showed significantly increased ratio of average weight of liver to body weight.

(3) After 18 months on diets with 25.0 ppm dieldrin, ♂ rats showed significant increase in ratio of kidney weight to body weight. No such effect at 2.5, 12.5 ppm. After 2 years exposure to 12.5 ppm, ♀ rats showed significant increase of kidney weight to body weight ratio.

(4) No deaths attributable to dieldrin occurred in the foregoing tests. Autopsied rats after 18 months and 2 years exposures showed minor liver cell changes.

(5) ♀, ♂ Rats, on diets with 300 ppm dieldrin (recrystallized), all died within 2 weeks; at 2.5, 5.0, 25.0, 75.0 ppm, mortality not significantly different from controls. Average periods of survival not significantly different from controls. 3128

h) Prolonged (> 15 month) feeding experiments with dogs: 3128, 3127

(1) Dogs proved more susceptible than rats to effects of dieldrin.

(2) Dogs, fed diets containing dieldrin at 1, 3 ppm, survived, without intoxication signs, the 15.7 months of experimental exposure. Growth rates of experimental, and control dogs (beagles) not significantly different. Livers significantly larger in experimental dogs, other organs normal; hematological findings normal. Vacuolation of distal renal tubules in one ♀ at 3 ppm; no histological abnormalities at 1 ppm. Dieldrin found in body fat at ca. 0.3-0.18 ppm.

(3) Dogs, receiving dieldrin in the diet at 25.0, 50.0 ppm, 6 days/week, died at intervals of from a few days to 1.3 months; at 10 ppm dogs survived for 9 months.

(4) Dogs, dead from dieldrin ingestion in the diet, showed diffuse, degenerative changes in brain, liver, kidneys.

Tabular summary (comparative). Dogs receiving Dieldrin, DDT, Lindane in diet: 3128

Insecticide	Dosage (Daily) mg/k	Dosage (Daily) ppm	Sex and Number	Exposure Time	Result
Dieldrin	9.8	50	♀, 1	5 days	Death.
Dieldrin	2.0-4.2	25-50	♀, 3; ♂, 1	11 day-1.3 mo.	Death.
Dieldrin	0.14-0.23	3	♀, 2; ♂, 2	15.7 mo.	Survival.
Dieldrin	0.033-0.10	1	♀, 2; ♂, 2	15.7 mo.	Survival.
DDT	1.2-2.5	30	♀, 2; ♂, 2	15.7 mo.	Survival.
DDT	0.45-0.81	10	♀, 2; ♂, 2	15.6 mo.	Survival.
Lindane	0.66-1.6	15	♀, 2; ♂, 2	15.6 mo.	Survival.

i) Effects of dieldrin on reproductive capacity of rats exposed for prolonged periods to dieldrin in the diet, (over 3 generations): 3128, 3126

(1) At 2.5 ppm in the diet, dieldrin reduced the number of pregnancies.

(2) Fed over several generations at 2.5, 12.5 ppm, the early evidence of pregnancy reduction tended to disappear.

(3) Severe effects upon the sucklings of dieldrin at 12.5, 25.0 ppm in the diet of mothers; slight to moderate effects at 2.5 ppm, measured as incidence of suckling mortality. Dieldrin, in the diet of parents, produced no effect on the weight of young alive at weaning.

Tabular, comparative summary, effect of dieldrin, others on reproduction, offspring:

	Highest Dosage Without And Lowest Dosage With Effect		
	Dieldrin	Aldrin	DDT
Deliveries, No.	< 2.5; 2.5	2.5; 12.5	25.0; > 25.0
Reduction in No. of pups/litter	25.0; > 25.0	25.0; > 25.0	25.0; > 25.0
Mortality of offspring (1-21 days)	2.5; 12.5	2.5; 12.5	2.5; 12.5
Weight of young (21 days)	25.0; > 25.0	25.0; > 25.0	25.0; > 25.0

j) Other data; chronic toxicity of dieldrin:

(1) Rats, receiving 25 ppm in the diet for 26 weeks, showed no demonstrable effects; at > 50 ppm degenerative liver changes appeared in exposures lasting to 26 weeks. 883

(2) Applied dermally to rabbits in amounts equal to 70 mg/k for over one week, dieldrin produced toxic symptoms; no comparable effects at 30 mg/k. 388

(3) Fed to rats at 5 ppm yielded no effect; at 25 ppm showed liver damage; at 50 ppm showed gross effects. Fed to dogs at 0.5 mg/k/day brought death in 2 of four subjects at 14, 201 days; at 1 mg/k/day 2 of 2 subjects dead at 83, 300 days; at 2 mg/k/day death of 2 of 2 subjects at 22, 35 days. 1953

(4) Chickens, 3-6 weeks old, receiving 50 ppm dieldrin, died within 90 days; at 25 ppm spasmodic feeding for a few weeks followed by return of appetite; all subjects dead in 6 months. 922

k) Subchronic toxicity, dieldrin for New Hampshire chickens: 2825

Concentration (ppm)	Mean % Mortality	Mean Wgt Gain (g) Survivors at 7 Wks.		Mean Food Consumption (g/chicken)		Efficiency Of Food Conversion To 3 Wks Of Age
		♂	♀	1 week	2 weeks	
50	17.5	682	576	121	174	2.2
25	0	801	648	130	189	2
12.5	2.5	808	680	135	185	2.1
6.25	0	832	704	140	195	2.0
0.0	0	843	704	133	192	2.0
Least Significant Difference (5%)		51	45	37	37	1.2
Least Significant Difference (1%)		67	59	51	51	1.6

3) Pharmacological, pharmacodynamical, physiological, etc.:

a) The immediate toxicity to rats, rabbits, of dieldrin, aldrin, endrin, isodrin by oral application is related more closely to spatial configuration than to empirical composition. Aldrin, isodrin and dieldrin, endrin are pairs of the same empirical composition; aldrin, dieldrin and isodrin, endrin in spatial configuration form closely related pairs: 3128

Comparative LD_{50} (mg/k)		
Aldrin dihydride	Rat ♀	420-620
Aldrin	Rat ♀	45.9
Aldrin	Rabbit	50-80
Dieldrin	Rat ♀	38.3
Dieldrin	Rabbit	45-50
Isodrin dihydride	Rat ♀	180-280
Isodrin	Rat ♀	16.4
Isodrin	Rabbit	5-7
Endrin	Rat ♀	16.8
Endrin	Rabbit	7-10

b) Dieldrin acts upon mammals as a central nervous stimulant and excitant. 89, 2231

(1) Precise mechanism of action unknown. 89

(2) CNS action results in: Increased reflex excitability, convulsions, brachycardia, vaso-depression, miosis; greatly reduces or eliminates appetite, the anorexia may precede or follow the nervous symptoms. For example, chickens on a diet containing 25 ppm of dieldrin, showed: Loss of appetite, extreme nervousness, alternate pupillary dilation, contraction, spasms accompanied by continuous squacking, circling, falling in opisthonus with stiff legs. Appetite may return in animals which are extremely affected and which eventually perish of dieldrin poisoning. 89, 1237, 1238, 922, 3127

(3) Three syndromes may be recognized, depending on size and number of doses: 89

(a) A few large doses: Yield increasing CNS stimulation culminating in one or more convulsions. Unless the animal dies, recovery, without permanent damage or great weight loss, is relatively prompt.

(b) Many doses of moderate size: Without warning may produce a complete loss of appetite, weight loss, convulsions. Without treatment death is seemingly inevitable.

(c) Many small doses: Yield one or few convulsions without any other apparent effect.

(4) Although the symptoms suggest a potentiation of acetylcholine effects on heart, intestine, there is no evidence of direct inhibitory action of dieldrin on choline esterase(s). 2231

(5) The parasympathetic effects are partly antagonized by atropine and barbiturates. 2231

c) Effects of dieldrin on man:

(1) The similarity in quantitative and qualitative effects noted in animals for dieldrin and aldrin seems to hold for man also. 89

(2) Exposure of human beings to oral doses of > 10 mg/k: Subjects become acutely ill. Symptoms may follow within 20 minutes; the latent period does not appear to exceed 12 hours. Permanent effects from non-fatal contact with dieldrin have not been noted. No quantitative data relating to chronic toxicity of dieldrin for man are recorded. 89

(3) Signs of intoxication in man include: 89

(a) Early symptoms of acute exposure: Headache, nausea, vomiting, dizziness, general malaise.

(b) In the more severe cases: Clonic, tonic, convulsions follow the early symptoms, or may appear as the primary evidence of intoxication. Coma may or may not follow. Hyperexcitability and excess irritability are common.

(c) In some spray operators repeated exposure has produced a condition indistinguishable from epilepsy. The seizures ended when the subjects' exposure to dieldrin ended. Intoxication, showing the characteristic symptoms of poisoning of a severe nature in animals, namely combined convulsions, complete appetite loss, severe weight loss, has not been reported for man.

d) Histopathology:

(1) In rats, the only characteristic histopathology was in the liver, with lesions characterized by hepatic cell swelling, cytoplasmic vacuolation, homogeneity and peripheral grouping of cytoplasmic granules. Altered cells may appear sporadically distributed in the liver, or may be moderate to quite numerous with concentration in the lobular mid-zone and central zone. Rats, on feeding experiments with dieldrin, showed a high incidence of infectious disease processes—chiefly of lungs, kidneys. 3125

(2) Histopathological findings in dogs, subjected to long term feeding tests at 3 ppm, could not, apparently, be related directly to the ingested insecticide. 3127 3128

e) The fate of dieldrin in the animal body: 175

(1) Evidence exists to indicate that aldrin is changed to dieldrin in the animal body by a rapid epoxidation. 175

(2) Dieldrin appears to remain unchanged in the animal body, and is recovered as such from animal products (e.g. milk, eggs) and body tissues (e.g. fat). 175

(3) Animals have shown convulsions as long as 120 days following the last dose of dieldrin, indicating the long persistence of the substance, or its derivatives, or the toxicant induced injury, once severe poisoning has occurred. 89

4) Effects of dieldrin on wildlife:

a) Feeding experiments with quail, pheasants; 780, 781

(1) Toxicity of dieldrin on continuous feeding to quail, pheasants: Animals numbering from 10 to 32 in each experimental group at each feeding level; number of controls no less than 96 up to 200 birds:

Bird	Age At Start Of Feeding	Dieldrin In Diet		Consumed (mg/k)		Mortality (%)	Survival Time (days)	Test Duration (days)
		%	ppm	daily	total			
Quail	Adult	0.5	5000	8.2	36.9	100	5	
Quail	Adult	.25	2500	10.2	46.2	100	5	
Quail	Adult	.125	1250	3.7	13.9	100	4	
Quail	Adult	.0625	625	5.0	19.3	100	4	
Quail	Adult	.010	100	2.8	15.3	100	6	
Quail	Adult	.005	50	0.9	5.8	100	7	
Quail	Adult	.001	10	0.8	31.1	100	39	
Quail	Adult	.0005	5	0.5	29.2	100	59	
Quail (control)	Adult					4.1	154	
Quail	Young, 1 day old	.002		1.14	25.0	100		40
Quail	Young, 1 day old	.001		1.19	58.4	100		60
Quail	Young, 1 day old	.0005		0.75	44.2	100		87
Quail	Young, 16 days old	.0005		0.81	46.2	100		76
Quail	Young, 1 day old	.001		1.87	13.1	75.0		7
Quail	Young, 1 day old	.0001		0.17	2.4	27.3		14
Quail	Young, 1 day old	.00005		0.11	0.8	0		7
Quail (control)	Young, 1 day old					28.5		90
Pheasant ♂	Adult	.01	100	2.4	24.0	100		10
Pheasant ♀	Adult	.01	100	2.0	62.0	100		31
Pheasant (cont.)	Adult					3.6		100
Pheasant	Young, 1 day old	.0005		0.53	47.7	100		90
Pheasant (cont.)	Young, 1 day old					31.5		120

(2) Effect on reproduction: Quail:

Dieldrin In Diet (%)	Eggs/Hen/Day (Av.)	Fertility (%)	Hatch (%)	Chicks Surviving At 1 wk	3 wks	12 wks
0.001	0.56	90.0	41.7	53.7	43.9	32.7
Control	0.53	88.6	82.3	90.0	87.5	78.3

(3) Effect of dieldrin by intermittent feeding to young quail:

	Initial Feeding				Second Feeding			
Dieldrin In Diet (%)	Duration (days)	Consumed (mg/k) daily	total	Mortality (%)	Duration (days)	Consumed daily	total	Mortality (%)
0.001	7	1.87	13.1	74.0	7	0.82	5.7	100
.0001	14	0.17	2.4	25.8	14	.09	1.2	100
.00005	7	0.11	0.8	0	7	.04	0.28	6.5
Control	7	—	—	4.0	—	—	—	—
Control	14	—	—	4.0	—	—	—	—
Control	7	—	—	22.0	—	—	—	—

(4) Effect of dieldrin on growth and survival of young quail: Dieldrin in diet at 0.0001%

Weeks On Test	Experimental Birds Survival (%)	Weight (g)	Control Birds Survival (%)	Weight (g)
1	91	12	96	16
2	91	24	96	26
3	91	48	96	50
4	91	66	90	70
5	91	82	82	90
6	34	100	78	110
7	0	—	78	124
8	—	—	78	130
9	—	—	78	155
10	—	—	78	163

(5) Effects of dieldrin fed during growth to quail and pheasant:

Bird	Dieldrin Fed (ppm)	Duration Test (days)	Mortality (%)	Consumed (mg/k) Daily	Total
Quail	20	40	100	1.6	62
Quail	10	61	100	1.2	70.2
Quail	5	76	100	0.7	50.2
Quail	5	87	100	0.6	49.6
Quail	1	76	100	0.8	46.2
Quail (control)	—	120	24.0	—	—
Pheasant	5	68	100	0.6	42.2
Pheasant (control)	—	103	28.0	—	—

(6) Effect of dieldrin fed during winter maintenance: Quail:

Dieldrin Fed (ppm)	Duration Test (days)	Mortality (%)	Consumed (mg/k) Daily	Total
1.0	162	17.5	0.12	19.4
0.5	162	0	0.08	13.0
Control	162	8.7	—	—

(7) Effect of dieldrin feeding on reproduction; quail and pheasant:

Bird	Dieldrin Fed (ppm) Winter	Reproduction	Mortality (%)	Av.Eggs/Hen	Fertility (%)	Hatch (%)	Chicks Surviving At End of 2 wks (%)	6 wks (%)
Quail	1.0	0	0	53	70.6	84.2	100	62.5
Quail	1.0	1.0	40	—	—	—	—	—
Quail	0	1.0	0	60	8.4	81.6	92.6	75.0
Quail (Control)	—	—	6.25	52	89.0	83.9	88.9	83.3
Pheasant	0	10.0	0	41	82.8	43.3	70.6	52.9
Pheasant	0	2.0	0	25	88.9	51.6	95.2	71.4
Pheasant	0	1.0	0	56	88.2	60.4	96.6	89.7
Pheasant (Control)	—	—	0	48	86.6	57.4	94.8	89.7

(8) Comparative toxicity of dieldrin and others to Bobwhite Quail and Mourning Dove; oral administration in gelatin capsules: 679

Compound	Quail				Dove			
	LD_{50} (mg/k)	MLD (mg/k)	Average Wgt. Loss (%)	Average Days Lived	LD_{50} (mg/k)	MLD (mg/k)	Average Wgt. Loss (%)	Average Days Lived
Dieldrin	12-14	10	20	4	44-46	40	15	3
Aldrin	4-4.5	4	15	3	15-17	12.5	18	4.5
Toxaphene	80-100	40	25	3	ca200-250	100	22	3
Lindane (♂)	120-130	120	25	3	ca350-400	200	10	2.5
Lindane (♀)	190-210							

5) Hazard:

a) Comparison of chronic oral toxicity per unit surface of Dieldrin, Aldrin, DDT as household and public health insecticides: 2547

Insecticide	LD_{50} (Rat) (mg/k)	Chronic Toxicity (ppm in daily diet)	Chronic Toxicity Ratio (DDT=1)	Common Dosage Public health Use mg/ft²	Dosage Ratio DDT = 1	Relative Chronic Toxicity/Unit Area
Dieldrin	65	25	2	25	0.125	0.25
Aldrin	50	25	2	50	0.25	0.5
DDT	250	50	1	200	1	1

b) Comparative chronic dermal toxicity per unit surface:

	Subacute Dermal Toxicity (mg/k)					
Dieldrin	40		3.8	25	0.125	0.5
Aldrin	20		7.5	50	0.25	1.9
DDT	150		1	200	1	1

c) Hazardous to fish and wildlife. Lakes, ponds, wildlife habitats should not be contaminated. 129

d) Residues are less than 0.1 ppm on crops at harvest, when applied according to dosage, application and time schedule recommended by manufacturer or formulator. 129

6) Phytotoxicity:

a) Said to be more phytotoxic than aldrin. More toxic, pound for pound, than DDT, chlordane, toxaphene, for most crops. However, the phytotoxic hazard is slight if dieldrin is properly formulated and used as recommended, even in dosages exceeding the normal. 294 129

b) Tends to persist in the soil; no harmful effect to microorganisms, no tainting of plants grown in soils treated even with excessive amounts. 129

c) The nature of the solvent in miscible or emulsifiable concentrates may influence markedly the phytotoxic hazard, particularly for tender plants and under such weather conditions as may prevent the rapid evaporation of the solvent. 2812

7) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aëdes taeniorhynchus (DDT-R)		CTC*	0.05-0.1 lb/acre	* = Concentration to control.	353
Anopheles quadrimaculatus (adult, 4 day) ♂	Topical	LD_{50}	.009 μg/insect	Relative effectiveness = 2.2 (DDT=1.0).	2051
" " " " ♀	Topical	LD_{50}	.023 μg/insect	" " = 2.9 (DDT=1.0).	2051
" " " " ♂	Topical	LD_{90}	.022 μg/insect	" " = 2.0 (DDT=1.0).	2051
" " " " ♀	Topical	LD_{90}	.048 μg/insect	" " = 2.7 (DDT=1.0).	2051
Apis mellifera (adult, worker)	or	LD_{20} 24 hr.	.223 μg/bee	In 50% sucrose solution.	1718
" " " "	or	LD_{50} 24 hr.	.269 μg/bee	" " " "	1718
" " " "	or	LD_{90} 24 hr.	.354 μg/bee	" " " "	1718
" " (" ")	Contact Spray	LD_{20} 24 hr	.386 μg/cm²	Av. deposit of 7.6 mg/cm² = 5.3 mg/bee.	1718
" " (" ")	Contact Spray	LD_{50} 24 hr	.575 μg/cm²	" " " " " " " " "	1718
" " (" ")	Contact Spray	LD_{90} 24 hr	1.052 μg/cm²	" " " " " " " " "	1718
" " (" ")	Contact Film	LD_{10} 24 hr	.04 μg/cm²	Exposure 1 hr; field av dose=.0014 mg/cm², 2 oz/acre.	1718
" " (" ")	Contact Film	LD_{90} 24 hr	.09 μg/cm²	" " " " " " " "	1718
" " (" ")	Fumig	LD_{0} 24 hr	.074 μg/cm²	Exposure 1 hr to vapors from dry films.	1718
" " (" ")	Fumig	LD_{100} 24 hr	.280 μg/cm²	" " " " " " " "	1718
Blabera fusca	inj	MLD < 7 da	1.5 μg/g	In acetone-triton solution.	1986
" "	inj	MTD*7 da	2.6 μg/g	*=Maximum tolerated dose. In acetone-triton.	1986
Blattella germanica (normal strain)	Topical	LD_{50} 48 hr	0.5 μg/insect		1012
" " (DDT-R)	Topical	LD_{50} 48 hr	0.62 μg/insect	Degree of resistance=1.2.	1012
" " adult (chlordane-R)	Topical	LD_{50} 48 hr	34.0 μg/insect	" " " =68	1012
" " ♀ (chlordane non-R)	inj	LD_{50}	6.59 μg/g	$\frac{LD_{50}\text{-R}}{LD_{50}\text{-non-R}} = 10.37$	431
" " " (Corpus Christi chlordane-R)	inj	LD_{50}	68.37 μg/g		431
					431

7) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Blattella germanica adult ♀ (chlordane non-R)	inj	LD_{90}	17.35 μg/g	$\frac{LD_{90}\text{-R}}{LD_{90}\text{-non-R}}$ = 28.54	431
" " " (Corpus Christi chlordane-R)	inj	LD_{90}	502.49 μg/g		431
					431
Chrysops discalis (adult)	Topical	LD_{50}(estimate)	.02 mg/fly		2707
" " "	Topical	LD_{90}	.95 mg/fly		2707
Fannia canicularis (adult) ♀	Topical	LD_{50} 24 hr	.003 μg/fly	In acetone.	1981
" " " ♂	Topical	LD_{90} 24 hr	.0026 μg/fly	"	1981
Melanoplus differentialis	or	LD_{50}	3.7 μg/g	Given as deposit on leaves.	3267
" "	Contact Sprays	LD_{50}	1.4 μg/g	Solution in organic solvents.	3267
" " (1, 2nd instar)	Contact Sprays	LD_{50}	.03 lb/acre	As emulsion sprays from emulsifiable concentrates.	1102
Melolontha melolontha	Contact	LD_{50} 5 da	1.6 μg/insect	Relative toxicity 0.4, BHC tech = 1.0.	3184
" "	Contact	LD_{80} 5 da	5.0 μg/insect	" " 0.5, " " "	3184
Mosquito larvae, various	Medium	CTCB* 62-78 wks	1 lb/acre	*=Conc. to control breeding; decidedly harmful to fish, other aquatic forms.	2135
Musca domestica (adult) NAIDM	Topical	LD_{50} 24 hr	1.1 μg/g	A laboratory strain of houseflies.	373
" " (") U of I	Topical	LD_{50} 24 hr	0.87 μg/g	" " " " "	373
" " (") DDT-I	Topical	LD_{50} 24 hr	2.4 μg/g	DDT-R strain 21 generations exposure, origin NAIDM.	373
" " (") DDT-W	Topical	LD_{50} 24 hr	1.3 μg/g	Field strain, 3 yrs. exp. to DDT.	373
" " (") DDT-III	Topical	LD_{50} 24 hr	1.0 μg/g	" " 4 " " " "	373
" " (") Methoxy-I	Topical	LD_{50} 24 hr	1.49 μg/g	21 generations exposure, origin NAIDM.	373
" " (") Lindane-I	Topical	LD_{50} 24 hr	2.66 μg/g	" " " " "	373
" " (") Multi-I	Topical	LD_{50} 24 hr	2.33 μg/g	8 " " " DDT-I strain.	373
" " (") Dieldrin-I	Topical	LD_{50} 24 hr	6.31 μg/g	21 " " " NAIDM.	373
" " (") Chlordane-I	Topical	LD_{50} 24 hr	1.9 μg/g	21 " " " "	373
" " (") Pyro-I	Topical	LD_{50} 24 hr	3.98 μg/g	21 " " " "	373
" " (") Multi-III	Topical	LD_{50} 24 hr	8.3 μg/g	8 " " " Methoxy-I strain.	373
" " (") Multi-II	Topical	LD_{50} 24 hr	7.1 μg/g	4 " " " " "	373
" " (larvae) NAIDM	Medium	Tolerated	1.2 ppm	Given in the larval medium.	373
" " (adult)	Topical	LD_{50}	1.1, 1.5 μg/g		2231
" " (") Laboratory strain	Contact	LD_{50} 24 hr	.019 μg/fly	At 80°F.	371
" " (")	Contact	LD_{50} 24 hr	> 100 μg/fly	After 36 generations exposure.	371
" " (") Laboratory strain	Contact	LD_{50} 24 hr	.031 μg/fly	At 60°F.	371
" " (") Bellflower (DDT-R)	Contact	LD_{50} 24 hr	.05 μg/fly	" "	371
" " (") Pollard (DDT-R)	Contact	LD_{50} 24 hr	.86 μg/fly	" "	371
" " (larvae 3rd instar)	Medium	LC_{50}	450(355-595)ppm	Measured by % pupal emergence.	666
" " (larvae)	Medium	?	5,10,20 mg/k	Medium gives 100% mortality.	1326
" " (larvae)	Medium	?	2 mg/k	" " 94% "	1326
" " (adult)	Contact Spray	LC_{50} 24 hr.	.017 mg/cc	KD 10 min at LC_{50} = 0.	2033
" " "	Space Spray	LC_{50}	.088 ± .011 mg/cc	Turntable, rel tox 32 (Pyrethrins = 1) 5.9 (Chlordane = 1)	1152
" " " (DDT-non-R)	Fumig	LT_{50}*	40 minutes	* - Lethal Time 50% at saturation.	3320
" " " (Orlando #1, DDT-R)	Fumig	LT_{50}*	110 minutes	" " " " "	3320
" " " (LDD, multi-R)	Fumig	LT_{50}*	550 minutes	" " " " "	3320
" " " (Ballard, lindane-R)	Fumig	LT_{50}*	550 minutes	" " " " "	3320
" " " (DDT-non-R)	Residual Deposit	LT_{50}*	< 1 minute	" " " " "	3320
" " " (Orlando #1)	Residual Deposit	LT_{50}*	9.1 minutes	" " " " "	3320
" " " (LDD)	Residual Deposit	LT_{50}*	> 120 minutes	" " " " "	3320
" " " ♀	Topical	LD_{50} 24 hr.	0.031 μg/fly	In acetone.	1981
Oncopeltus fasciatus	Topical	LD_{50}	15.0 μg/g		2231
" " (adult ♀)	inj	LD_{50} 24 hr.	6.9 μg/g	Recryst., in acetone; tox ratio 4.5 (DDT = 1)	348
" " " "	inj	LD_{90} 48 hr.	3.8 μg/g	" " " " " 2.9 " "	348
" " " "	inj	LD_{95} 24 hr.	61.0 μg/g	" " " " " 17.1 " "	348
" " " "	inj	LD_{95} 48 hr.	39.0 μg/g	" " " " " 11.2 " "	348
Periplaneta americana	Topical	LD_{50}	1.5 μg/g		2231
" " (adult ♀)	inj	LD_{50} 96 hr	5.0 μg/g	LD_{50}♀ / LD_{50}♂ = 5; In xylol, acetone, deobase, ethanol	558
" " (" ♂)	inj	LD_{50} 96 hr.	1.0 μg/g	10:10:75:5	558
Protoparce sexta (5th instar)	Topical	LD_{50}	487.0 μg/insect	Large larvae 5.4 (4.1-7.5) g.	1306
" " " "	Topical	LD_{90}	2559.0 μg/insect	" " " " " "	1306

b) Comparative toxicity, dieldrin and other insecticides:

(1) Chemotherapeutic value, dieldrin and other compounds, for insects undergoing larval development within leaves of plants. As sprays, vs. Monarthropalpus buxi, Phytomyza ilicis (Boxwood and holly-leaf miners): 1782

Material	M. buxi			P. ilicis	
	Lbs/100 gal.	Applications No.	Surviving Larvae (%)	Lbs/100 gal.	Surviving Larvae (%)
Dieldrin 25% wettable powder	4	1	11.2	4	7.8
" "	"	2	11.5	—	—

b) Comparative toxicity, dieldrin and other insecticides:

(1) Chemotherapeutic value, dieldrin and other compounds, for insects undergoing larval development within leaves of plants. As sprays, vs. *Monarthropalpus buxi*, *Phytomyza ilicis* (Boxwood and holly-leaf miners): 1782

Material	*M. buxi*			*P. ilicis*	
	Lbs/100 gal.	Applications No.	Surviving Larvae (%)	Lbs/100 gal.	Surviving Larvae (%)
Aldrin 25% wettable powder	4	1	30.8	4	6.2
" "	"	2	35.6	—	—
DDT 50%	2	1	68.0	—	—
" "	"	2	61.5	—	—
BHC 50%	2	1	70.4	—	—
" "	"	1	62.1	—	—
Lindane 25% "	4	1		4	82.0
Chlordane 50% "	2	1	7.9	—	—
" "	"	1	69.0	—	—
" 40% "	2.5	1		2.5	82.5
Nicotine sulfate 40%	2.5	1	65.5	—	—
" " "	"	2	61.8	—	—
Control			76.7		92.6

Least Significant Difference 5% = 12.0% LDS 5% = 8.3%

(2) Vs. *Fanusa pusilla* (2nd generation; Birch leaf miner): 1782

Material	Lbs/100 gal	Applications	Days After Adult Emergence	Leaves With Living Larvae (%)
Dieldrin 25% wett pwdr	2	3	10, 17, 24	0
" "	2	2	10, 17	0
" "	2	1	10	6.3
Aldrin "	2	3	10, 17, 24	0
" "	2	2	10, 17	1.7
" "	2	1	10	22.0
Chlordane 40%	2.5	3	10, 17, 24	18.2
" "	2.5	2	10, 17	21.2
" "	2.5	1	10	25.9
Nicotine sulfate 40%	1 pint	3	10, 17, 24	2.4
" "	1 pint	2	10, 17	8.3
" "	1 pint	1	10	29.5
Control	—			96.3

(3) Comparative toxicity dieldrin and other compounds for *Melanoplus differentialis*: 3267

Insecticide	LD$_{50}$ (μg/g)	
	Contact	Oral
Dieldrin	1.4	3.7
Parathion	0.8	8.9
Aldrin	1.8	2.3
Heptachlor	1.6	4.4
Lindane	3.4	6.7
Chlordane	9.8	12.0
Toxaphene	61.0	91.5

(4) Degree of control of *Pyrausta nubilalis* achieved with dieldrin and other compounds: 675

Insecticide	Lbs/Gal	% Reduction Of *P. nubilialis*	
		As Direct Spray	As Residual Deposit
Dieldrin	0.5	78	49
DDT	1.0	54	40
DFDT	1.0	64	73
Aldrin	0.75	70	74
Heptachlor	1.0	70	77
EPN	0.75	57	79
Parathion	0.5	65	18

(5) Toxicity of dieldrin and other compounds for Anopheles quadrimaculatus, 4 day adults; topical application: 2051

Insecticide (ethanol sol)	LD$_{50}$ (μg/insect)		LD$_{90}$ (μg/insect)		Relative Effectiveness (DDT = 1)*			
					At LD$_{50}$		At LD$_{90}$	
	♂	♀	♂	♀	♂	♀	♂	♀
Dieldrin	.009	.023	.022	.048	2.2	2.9	2.0	2.7
p,p'-DDT	.020	.066	.045	.13	*1.0	*1.0	*1.0	*1.0
p,p'-TDE	.041	.1	.098	.22	.49	.66	.46	.59
Methoxychlor (tech.)	.035	.1	.078	.22	.57	.66	.58	.59
Chlordane	.105	.24	.19	.46	.19	.28	.24	.28
Lindane	.0085	.011	.032	.042	2.4	6.0	1.4	3.1
Toxaphene	.15	.29	.29	.5	.13	.23	.16	.26
Malathion	.0087	.0095	.019	.022	2.3	7.0	2.4	5.9
Allethrin	.0029	.008	.013	.041	6.9	8.3	3.5	3.2

(6) Comparative toxicity for Protoparce sexta (larva) of dieldrin and other compounds: 1306

Small larvae (=S)	0.9 (.6-1.1)g	2, 3 instar
Medium larvae (=M)	2.5 (1.2-4)g	3, 4 instar
Large larvae (-L)	5.4 (4.1-7.5)g	5 instar

Insecticide	Size Larva	Topical Application	
		LD$_{50}$ (μg/larva)	LD$_{90}$ (μg/larva)
Dieldrin	L	482	2559
Endrin	L	42	219
Parathion	L	52	183
Isodrin	L	87	490
Lindane	L	206	1235
Malathion	L	481	1276
Aldrin	L	487	1359
Heptachlor	L	1058	4005
Toxaphene	L	1363	5778
DDD	L	2622	9813
DDT	L	$\gg$ 4000	

(7) Comparative toxicity vs. Musca domestica of dieldrin and other insecticides:

(a) As contact sprays applied by turntable modification of Peet-Grady method. 2033

Insecticide	Concentration for 50% Mortality, 24 hrs. (%)	10 Minute KD At LC$_{50}$ 24 hrs. (%)
Dieldrin	0.017	0
Parathion	.02	0
Methyl parathion	.025	0
Lindane	.046	0
Heptachlor	.052	0
Aldrin	.056	0
TEPP	.069	ca 70
Chlordane	.25	0
DDT	.35	0
Malathion	.48	0
Toxaphene	.68	0
Tetrapropyl dithiopyrophosphate	.69	0
Dilan	.72	ca 30
Isolan	1.15	100
Allethrin	1.5	100
Pyrolan	5.5	100

(b) Applied as space sprays (Campbell Turntable Method) vs. adult Musca (100/test) insecticides in kerosene solution: 1152

Insecticide	Conc. (mg/cc)	KD 25 min. (%)	Mean Kill 24 hrs (%)	LC$_{50}$ (mg/cc)	Relative Toxicity Compared To:	
					Pyrethrins =1	Chlordane =1
Dieldrin	.25	5	98			
	.125	1	74	.088 ± .011	32	5.9
	.063	2	27			
Chlordane (tech) sample A	1.0	8	99			
	.5	7	74	.33 ± .04	4.2	1.0
	.25	11	33			
Chlordane (tech) sample B	1.0	9	93			
	.5	11	70	0.39 ± .05	3.5	1.0
	.25	6	20			

(b) Applied as space sprays (Campbell Turntable Method) vs. adult *Musca* (100/test) insecticides in kerosene solution: 1152

Insecticide	Conc.(mg/cc)	KD 25 min (%)	Mean Kill 24 hrs (%)	LC_{50} (mg/cc)	Relative Toxicity Compared To Pyrethrins	Relative Toxicity Compared To Chlordane
Heptachlor	.5	14	100			
	.25	8	100			
	.125	7	73			4.0
	.25	4	93			
	.125	5	45	.119±.009	28	4.4
	.063	7	17			
Chlordane tech. sample A	1.0	10	84			
	.5	3	51	.52 ±.039	6.4	1.0
	.25	6	12			
Chlordane crystalline	1.0	9	66	.743±.055		.7
	.5	9	28			
	.25	6	11			
Pyrethrins	2.0	100	71	1.37±0.16	1.0	
	1.0	100	32			
	8.0	100	82	3.32±0.25	1.0	
	4.0	100	58			
	2.0	100	26			
	1.0	100	13			
	4.0	100	63	2.83±0.36	1.0	
	2.0	100	36			
	1.0	100	17			
Aldrin	.25	7	85	.131±.01	25	4.0
	.125	8	45			
	.063	9	15			
	.25	5	82	.129±.017	22	4.0
	.125	6	51			
	.063	3	15			

N.B. Variations in resistance and susceptibility of various *Musca* "populations".

(c) Toxicity of vapors and residues of dieldrin and other compounds for various resistant and non-resistant strains of *Musca*, expressed as LT_{50} (time in minutes for 50% mortality): 3320

Insecticide	LT_{50} (minutes) Vapors non-R	Orlando #1*	LDD**	Ballard ***	Residues non-R	Orlando #1*	LDD**	Ballard***
Dieldrin	40	110	550	550	< 1	9.1	> 120	—
Chlordane	33	69	347	380	—	—	—	—
Lindane	25	58	173	316	10.9	16.4	65.6	229.3
Aldrin	< 15	23	158	96	—	—	—	—
DDT	—	—	—	—	9.0	ca 1440	> 240	343.4

* Orlando #1: Exposed only to DDT; high resistance developed, some cross resistance to lindane, dieldrin, chlordane.

** LDD: Strain from a dairy where DDT, dieldrin, lindane would not control. Resistance maintained by contact cage exposure in insectary.

*** Ballard: Wild strain from dairy where space and residual lindane had relative lack of effect.

(d) Dieldrin and other insecticides, used as insecticidal emulsions to control *Musca* larvae. Laboratory Tests. (Field experience far less encouraging): 1326

Insecticide	% Mortality At 50 mg	20 mg	15 mg	10 mg	5 mg	2 mg
	(mg active ingredient/K medium)					
Dieldrin	—	100	—	100	100	94
DDT	100	—	—	—	—	—
Methoxychlor	25	—	—	—	—	—
Toxaphene	100	100	—	100	75	0
Lindane	—	99.5	—	60	—	—
Chlordane	—	—	100	—	—	75
Aldrin	—	—	100	100	100	97.5
Heptachlor	—	100	—	—	100	90
Dilan	99.5	100	—	100	5	—

(e) Comparative toxicity of dieldrin and other compounds, incorporated in larval medium, for 3rd instar Musca larvae; as measured by % pupal emergence compared with controls: 666

Insecticide	LD_{50} (ppm)	.95 Fiducial Limits (ppm)	
Dieldrin	450	355-595	No statistically significant difference.
Aldrin	430	340-595	
Endrin	125	100-160	
Chlordane	1450	1100-1900	
DDT	2300	1600-3300	

(f) Dieldrin and other compounds, used as baits for control of Musca (adults); laboratory and field: 1915

Insecticide	Laboratory Tests % Down Or Dead In			Field
	30 min	1 hr	24 hrs	Control After 24 hrs
Dieldrin (1%)	20	66	100	Unsatisfactory
Aldrin (1%)	20	76	100	—
BHC (1%)	43	76	100	—
Chlordane (1%)	10	20	100	—
DDT (1%)	30	44	98	Unsatisfactory
Heptachlor (1%)	6	48	100	Unsatisfactory
Lindane (1%)	3	6	100	Unsatisfactory
Methoxychlor (2%)	23	20	93	Unsatisfactory
Strobane (1%)	10	36	96	—
Toxaphene (1%)	40	56	100	Unsatisfactory

(g) Comparative toxicity dieldrin and other compounds for Chrysops discalis. Topical application: 2707

Insecticide	LD_{50} (estimate) (μg/fly)	LD_{90} (μg/fly)
Dieldrin	20	950
Lindane	4	35
Endrin	9	80
DDT	20	250
Methoxychlor	30	90
Aldrin	40	170
Heptachlor	40	200
EPN	48	120
Isodrin	60	170
Chlordane	60	650
Bayer 22/190	65	420
Diazinon	90	360
Malathion	130	330
Toxaphene	180	480

(8) Comparative toxicity dieldrin and other compounds, vs. Melolontha melolontha (DDT inefficacious): 3184

Insecticide	LD_{50} 5 day	LD_{80} 5 day	Relative Toxicity At (BHC = 1)	
	μg/ insect		LD_{50}	LD_{80}
Dieldrin	1.6	5	0.4	0.5
BHC (tech)	.7	2.5	1.0	1.0
Aldrin	2.7	> 6	.25	< .4
Chlordane	9	20	.08	.12
Toxaphene	ca 7	ca 20	ca .1	ca .12

(10) Comparative toxicity of dieldrin and other compounds vs. grasshoppers:

(a) Grasshoppers fed on cabbage leaves, field-sprayed at 4 oz Aldrin/48 gal U.S., 2 oz Dieldrin/48 gal U.S.; leaves removed and fed to insects at 1, 3, 5 days after treatment: 2281

Grasshopper	Days After Spraying Leaves Fed	Aldrin (% Kill)		Dieldrin (% Kill)	
		24 hrs	48 hrs	24 hrs	48 hrs
Camnula pellucida	1	73.9	100	96	100
	3	84.0	100	78.3	95.4
	5	83.4	100	95.5	100
Melanoplus bivittatus	1	45.8	86.5	87.5	100
	3	40.0	100	64.0	100
	5	31.8	96	67.9	100
Melanoplus mexicanus	1	52.2	78.3	82.7	100
	3	.1	79.2	61.5	96
	5	15.4	85.4	96.3	100

(b) Dieldrin and other compounds in cornfield tests vs. Sphaenarium purpurascens: 307

Insecticide	Dust Conc. (%)	Active lb/acre	% Mortality After 12 hrs	% Mortality After 24 hrs
Dieldrin	1	.35	74.2 (68-80)	98.2 (96-100)
Dieldrin	2.5	.88	89.8 (87-93)	99.8 (99-100)
Aldrin	1	.32	77.8 (69-88)	97.8 (95-100)
Aldrin	2.5	.82	88.6 (83-96)	99.6 (99-100)
BHC	1	.36	86.6 (78-92)	94.2 (90-97)
BHC	2.5	.85	93.0 (89-98)	97.0 (93-100)
Isodrin	.5% spray	.43	83.2 (81-92)	91.4 (80-96)
Toxaphene	5	1.74	26.8 (18-36)	53.0 (46-60)
Toxaphene	10	3.6	40.4 (36-47)	61.4 (55-69)
Parathion	.5	.16	43.6 (36-51)	69.4 (61-80)
Parathion	1.0	.35	66.8 (59-80)	76.0 (69-84)
Chlordane	2.5	.95	32.0 (27-39)	46.6 (41-54)
Chlordane	5.0	1.8	49.6 (39-62)	63.8 (50-77)
Endrin	.5% spray	.36	32.8 (24-40)	47.6 (43-59)

(c) Comparative toxicity of dieldrin and other compounds vs. Melanoplus differentialis: 3267, 1102

Insecticide	M. differentialis (adults) *Contact LD_{50} (μg/g) [3267]	M. differentialis (adults) **Oral LD_{50} (μg/g) [3267]	1st, 2nd Instar Nymphs LD_{50} (Lbs active/acre) [1102]
Dieldrin ***	1.4	3.7	.03
DDT	> 3300, 9380	> 1350, 2579.0	—
DDT	—	1170.0 (colloidal susp., applied to mouth parts)	
Aldrin ***	1.8	2.3	.04
BHC	—	—	.04
Lindane	1.6, 3.4	6.6, 6.7	.08
Chlordane	16.3, 9.8	21.8, 12.0	.49
Heptachlor	2.6, 1.6	6.0, 4.4	—
Toxaphene	73.9, 61.0	75.0, 91.5	.91
Parathion (tech)	0.7, 0.8	6.0, 8.9	.05
TEPP	4.4	—	—
HETP	18.4	—	—

* Insecticides in solution in dioxane, ethanol.

** Given as deposits on leaves.

*** At 2 oz/acre gave control comparable to chlordane, toxaphene at much higher rate; at 0.3 lb/acre gave complete control comparing with chlordane, toxaphene at 1 lb/acre.

(11) Dieldrin and other insecticides vs. Aëdes dorsalis, Aëdes vexans larvae, pupae; laboratory tests at 75°F in distilled H_2O: 2282 2283

Insecticide	% Mortality 24 Hrs At 1 ppm larvae	At 1 ppm pupae	At 1:2,000,000 larvae	At 1:2,000,000 pupae	At 1:5,000,000 larvae	At 1:5,000,000 pupae	At 1:10,000,000 larvae
Dieldrin	100	79	96.9	78	99	63	95
Aldrin	100	75	96.9	30.4	99	34	95
DDT	100,87	6	96.9	30	100	8.2	98
Endrin	100	95	98.9	99	98	61	98
Isodrin	100	78.8	98.0	70	97	58	81
Toxaphene	96		93.0	2.3	91	2.7	84
Control	15.2	2.4	—	—	—	—	—

(12) Comparative toxicity dieldrin and other compounds for certain resistant and non-resistant strains of Blattella germanica adult ♀ ; topical application: 1012

Insecticide	LD_{50} μg/insect Normal Strain	DDT-R Strain LD_{50} (μg/insect)	DDT-R Strain Resistance Degree	Chlordane-R Strain LD_{50} (μg/insect)	Chlordane-R Strain Resistance Degree
Dieldrin	0.5	0.62	1.2	34.0	68
DDT	13.5	25.0	1.9	19.0	1.4
Chlordane	2.3	4.1	1.8	250.0	108.6
Diazinon	0.33	0.78	2.4	0.4	1.2
Allethrin (synergized)	0.76	1.3	1.7	1.0	1.3

(13) Comparative toxicity, dieldrin and other compounds, for chlordane non-R and Chlordane-R (Corpus Christi) strains of Blattella germanica (adult ♀): 431

Insecticide	Non-R Strain		Chlordane-R Strain		Degree of Resistance	
	LD_{50} (μg/g)	LD_{90} (μg/g)	LD_{50} (μg/g)	LD_{90} (μg/g)	At LD_{50}	At LD_{90}
Dieldrin	6.59	17.35	68.37	502.49	10.37	28.54
Aldrin	26.46	70.06	127.61	1113.6	4.82	15.89
Chlordane	81.29	144.27	1117.5	4648.8	13.76	32.22
Heptachlor	9.07	19.85	174.21	1509.3	19.21	76.04
Lindane	1.01	2.57	23.13	75.02	22.72	29.19

(14) Comparative sex difference in susceptibility of adult Periplaneta americana to dieldrin and other compounds; applied by injection, dissolved in a mixture of xylene, acetone, deobase, absolute ethanol 10: 10: 75: 5 . 558

Insecticide	♂ LD_{50} 96 Hrs (μg/g)	♀ LD_{50} 96 Hrs (μg/g)	LD_{50} ♀ / LD_{50} ♂ (Ratio)
Dieldrin	1.0	5.0	5
Lindane	0.8	4.4	5.5
DDT	4.5	20.0	4.4
Toxaphene	25.0	80.0	3.2
Chlordane	26.0	52.0	2.0
Methoxychlor	7.0	18.0	2.5

(15) Comparative toxicity dieldrin and other compounds for Oncopeltus fasciatus, adult ♀; by injection (insecticides recrystallized, applied in acetone solution): 348

Insecticide	*LD_{50} 24 Hrs	*LD_{50} 48 Hrs	*LD_{95} 24 Hrs	*LD_{95} 48 Hrs	Toxicity Ratio			
	μg/g				At LD_{50} 24 Hrs	LD_{50} 48 Hrs	LD_{95} 24 Hrs	LD_{95} 48 Hrs
Dieldrin	6.9	3.8	61.0	39.0	4.5	2.9	17.1	11.2
Aldrin	4.5	2.5	72.0	43.0	6.9	4.6	14.5	10.2
p,p′-DDT	31.0	11.0	1043.0	437.0	**1.0	**1.0	** 1.0	** 1.0

* = calculated from regression equations derived from average mortalities of 3 replicates involving 5700 O.fasciatus.

** = standard, DDT = 1

(16) Comparative speed of toxic action, dieldrin and other compounds vs. Macrosiphum pisi on Vicia faba, as dusts in talc; application in a dusting tower: 520

Insecticide	Conc. (%)	Temp. (°F)	Time For			
			50% Kill		98% Kill	
			Hrs.	Min.	Hrs.	Min.
Dieldrin	1	75	4	7	6	43
Toxaphene	5	72	13	20	19	1
Chlordane	5	72	9	24	18	8
EPN	.86	74	5	26	8	6
Aldrin	1	75	3	44	7	32
DDD	5	72	2	34	4	35
Methoxychlor	10	75	2	1	5	34
Parathion	1	70	1	8	1	43
	2	70	1	21	1	53
DDT	5	72	0	57	1	45
Lindane	1	72	0	56	1	54
Rotenone	5	72	0	47	1	23
TEPP	.18	74	0	20	0	56
Nicotine	1	72	0	15	1	12
Nicotine	3	72	0	12	0	50
Talc (alone)		67-72	13	28	23	51

(17) Comparative toxicity in field tests of dieldrin and other compounds vs. Leptinotarsa decemlineata, 3rd Instar: 1986

Insecticide	Dusts				Sprays			
	g/k	g/hectare	% Survival At		g/100 l	g/hectare	% Survival At	
			24 Hrs	48 Hrs			24 Hrs	48 Hrs
Dieldrin	12.5	354	0	0	10	67	7	0
Dieldrin	6.0	164	8	0	—	—	—	—
Dieldrin	3.0	85	18	0	—	—	—	—

(17) Comparative toxicity in field tests of dieldrin and other compounds vs. Leptinotarsa decemlineata, 3rd Instar: 1986

Insecticide	Dusts g/k	Dusts g/hectare	Dusts % Survival At 24 Hrs	Dusts % Survival At 48 Hrs	Sprays g/100 l	Sprays g/hectare	Sprays % Survival At 24 Hrs	Sprays % Survival At 48 Hrs
Chlordane	50	1485	1	0	50	316	34	24
Heptachlor	50	1228	8	4	10	76	100	80
Heptachlor	22	624	38	12	20	118	66	26
Heptachlor	12.5	291	57	37	—	—	—	—
Aldrin	12.5	260	2	0	10	76	88	72
Aldrin	6.0	184	52	24	20	136	32	22
Aldrin	3.0	92	66	48	—	—	—	—
Isodrin	25.0	604	0	0	10	65	46	2
Isodrin	12.5	395	20	0	—	—	—	—
Isodrin	6.0	175	26	0	—	—	—	—
Isodrin	3.0	97	62	46	—	—	—	—
Endrin	25.0	686	0	0	10	72	2	0
Endrin	12.5	468	12	0	—	—	—	—
Endrin	6.0	184	22	0	—	—	—	—
Endrin	3.0	82	78	48	—	—	—	—

(18) Comparative toxicity dieldrin and other compounds for Anasa tristis in laboratory tests; topical application in acetone solution, adult insects: 3376

Insecticide	% Mortality 72 Hrs At Indicated Dosages (µg/g) 32	64	128	256	512	% Mortality After 30 Min Exp To Surfaces Treated 7 Days Previously At 100 mg/ft^2 24 Hrs	48 Hrs	72 Hrs	96 Hrs
Dieldrin	—	—	70	100	100	30	80	80	100
Parathion	100	100	100	100	100	10	10	20	40
Lindane	83.3	100	100	100	100	10	20	20	20
Aldrin	—	93.3	100	100	100	0	0	0	0
Endrin	—	—	100	100	100	—	—	—	—
EPN	—	—	100	100	100	—	—	—	—
Heptachlor	—	83.3	90	100	100	0	10	20	20
Isodrin	—	—	90	100	100	—	—	—	—
Chlordane	—	—	36.7	80	90	—	—	—	—
Toxaphene	—	—	16.7	66.7	82	—	—	—	—
DDT	—	—	20	30	76.7	—	—	—	—

Rates of action at lowest dosage (topical) yielding 90% (or better) kills in 72 hrs of Anasa tristis:

Insecticide	(µg/g)	% Mortality At 12 Hrs	24 Hrs	48 Hrs	72 Hrs
Dieldrin	256	0	70	96.7	100
Parathion	6	3.3	33.3	76.7	90
Lindane	64	—	80	100	100
Aldrin	64	—	23.3	76.7	93.3
Endrin	128	6.7	20.0	80.7	100
EPN	128	10	26.7	76.7	100
Heptachlor	128	10	50	80	90
Isodrin	128	0	10	63.3	90
Chlordane	512	—	6.7	73.3	90

(19) Toxicity of dieldrin and other compounds for Conotrachelus nenuphar (adult) topically treated by wetting in water suspensions of the toxicants and by exposure to insecticide residues: 2864

Toxicant	LC$_{50}$ (ppm)	Ratio to Parathion	Field Conc. (ppm)	Minimum Effective Residue (mg/100 cm^2)	Ratio to Parathion
Dieldrin	104	7.4	300	71	2.1
Parathion	14	1.0	360	34	1.0
EPN®	32	2.3	390	68	2.0
Methoxychlor	4000	285.7	1800	865	25.4

(20) Dieldrin and other compounds comparative toxicity for Cirphis unipuncta (larva): 3268

Toxicant	Topical Application LD$_{50}$ µg/g	Topical Application Ratio to Parathion	Oral (on treated leaves) LD$_{50}$ µg/g	Oral (on treated leaves) Ratio to Parathion	Ratio LD$_{50}$: LD$_{99}$ Topical	Ratio LD$_{50}$: LD$_{99}$ Oral
Dieldrin	8.3	2.2	4.6	1.8	3.1	3.8
Parathion	3.7	1.0	2.5	1.0	3.4	8.5
DDT	193.0	52.2	45.7	18.3	4.7	22.8
Chlordane	117.5	31.6	78.2	31.3	4.9	4.7

(20) Dieldrin and other compounds comparative toxicity for *Cirphis unipuncta* (larva): 3268

Toxicant	Topical Application		Oral (on treated leaves)		Ratio LD_{50} : LD_{99}	
	LD_{50} μg/g	Ratio to Parathion	LD_{50} μg/g	Ratio to Parathion	Topical	Oral
Toxaphene	56.2	15.2	34.1	13.6	4.7	2.9
Lindane	28.1	7.6	27.9	11.2	3.2	5.1
Aldrin	19.8	5.4	11.4	4.6	3.7	24.7
Dilan	8.8	2.4	11.5	4.6	5.4	5.0

c) Comparative toxicity, dieldrin and other compounds for certain beneficial insects:

(1) Honeybees, *Apis mellifera*: 1718

Order of effectiveness: As stomach, contact poisons:

Parathion > TEPP > lindane > dieldrin > aldrin > chlordane ≥ Systox® > BFPO > toxaphene

As residual films

Dieldrin > aldrin > lindane > parathion > chlordane > Systox®; no effect with (toxaphene, TEPP, BFPO)

As fumigants

Dieldrin > lindane > aldrin > parathion > chlordane; no effect with (Systox®, BFPO, TEPP, toxaphene)

Insecticide	Oral Dosage (μg/bee) To Give Mortality 24 Hrs.			Contact Spray (μg/cm^2) To Give Mortality 24 Hrs.			Dry Film (μg/cm^2) Yielding Vapors To Give Mortality 24 Hrs.	
	20%	50%	90%	20%	50%	90%	100%	0%
Dieldrin	.223	.269	.354	.386	.575	1.052	.280	.074
Parathion	.018	.04	.144	.257	.354	.574	5.0	2.8
TEPP	.052	.065	.093	.358	.445	.621	—	5.5
Lindane	.026	.079	.346	.772	.851	.986	.44	.28
Aldrin	.181	.239	.365	.327	.562	1.274	.74	.074
Chlordane	.831	1.122	1.73	3.802	5.0	7.58	3.7	.37
Systox®	1.255	1.478	1.884	4.321	5.123	6.619	—	18.5
Dimefox®	1.25	1.905	3.506	16.52	23.17	38.64	—	74.0
Toxaphene	25.12	104.50	186.66	36.73	44.67	59.98	—	70

For *Apis mellifera* in contact for 1 hour with residual films:

Insecticide	% Kill 24 Hrs	Dry Film (μg/cm^2)	Field Average Dose μg/cm^2	Ounces/Acre; Av. Dose
Dieldrin	90	0.09	1.4	2
Dieldrin	10	.04		
Aldrin	75	.09	1.4	2
	0	.04		
Lindane	100	.28	2.8	4
	0	.074		
Parathion	90	.54	1.4	2
	10	.18		
Chlordane	100	3.40	11.2	16
	12	.90		
Systox®	50	10.0	—	
	22	6.8		
TEPP	8	0.22	5.6	8
Toxaphene	9	110.0	16.8	24
	0	40.0	—	
Dimefox	0	50.0	—	—

(2) Comparative toxicity dieldrin and other compounds for 3 beneficial insects; adult insects placed on plants previously dusted by vacuum dusting method: 1404

Dust Concentration		% Mortality 24 Hrs Of		
		Collops vittatus	*Hippodamia convergens*	*Coleomegilla maculata*
Dieldrin	(2%)	36	4	24
DDT	(5%)	38	6	32
Perthane	(5%)	23	6	12
Strobane	(5%)	10	18	12
Heptachlor	(2.5%)	41	30	38
Toxaphene	(10%)	32	12	36
Endrin	(1%)	27	10	18
Parathion	(2%)	65	78	98
Malathion	(5%)	47	90	100
Chlorothion	(5%)	64	82	100
Diazinon	(4%)	37	66	100
Control		11	4	0
Lowest Significant Difference	(5% level)	20	24	26

d) Some reports of effectiveness of dieldrin in field control of economically important insects; field experiences:
  - (1) Vs. Empoasca: Ineffective 2280
  - (2) Vs. Protoparce sexta: Effective control. 821
  - (3) Vs. Heliothis armigera: Inferior to DDT in control of. 158
  - (4) Vs. Melittia satyriniformis: Partly effective as soil insecticide. Inferior to lindane. 1614
  - (5) Vs. Hylemyia antiqua, H. brassicae, H. floralis, H. cilicrura, H. trichodactyla: Effective in control. 353, 1800
  - (6) Vs. Dacus dorsalis: 10 times as effective as DDT in control of on mangoes. 489
  - (7) Vs. Limonius spp: 5 lbs/acre protects potatoes without risk of tainting. 353
  - (8) Vs. Leptinotarsa decemlineata: A 0.025% suspension = in effect to 0.1% DDT suspension. 2280
  - (9) Vs. Hylastinus obscurus: Most effective for; in order dieldrin > BHC > aldrin. 1313
  - (10) Vs. Anthonomus grandis: = in effect to aldrin; both are of choice. 1657
  - (11) Vs. Conotrachelus nenuphar: Highly toxic for adults; superior to aldrin in control of; parathion > aldrin 275
    = dieldrin = chlordane > BHC. 517
  - (12) Vs. Acarines: Dieldrin possesses acaricidal properties. 1757
  - (13) Vs. Amblyomma americanum: More effective than aldrin, lindane, DDT, chlordane, in field control of. 3073
  - (14) Vs. Simulium spp.: Inferior to DDT as a larvicide for. 1549
  - (15) Vs. Musca domestica (and other flies): 10 times as toxic as tech. chlordane; lacking in "KD" power. 1152
  - (16) Vs. Prodenia litura: on cotton (Egypt), 2.5% dusts yielded 100% kill of larvae in 24 hours. 930
  - (17) Vs. Mosquitoes: Most effective of four insecticides used vs larvae; 1 lb/acre controlled breeding for 62-78 weeks. 2135

e) For screening test data showing high effectiveness of dieldrin vs. lice, mosquitoes, flies, fleas, cockroaches, consult Ref. 1801.

8) Pharmacological, pharmacodynamical, physiological etc.; insects:

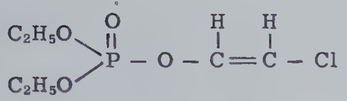
a) Superficially the effect of dieldrin on insects is DDT-like (as are the effects of other cyclodiene insecticides). 2231
  - (1) The neurotoxic symptoms do not (as is true also of chlordane, toxaphene, aldrin, other chlorinated terpenes) appear until the passage of a marked latent period. 353
  - (2) The sharp rise in O_2 consumption (almost immediate in the case of DDT, methoxychlor, lindane, p-dichlorobenzene, TEPP, dichloroethyl ether, pyrethrins, nicotine, azobenzene, dinitro-compounds) does not take place until the passage of from 30 minutes to 6 hours, with the insect passive in the interim. 353
  - (3) Blattella germanica injected with dieldrin (10 μg/insect) showed a latent period of several hours then a sudden rise in O_2 consumption to 5-6 times the normal. Hyperactivity was an accompanying symptom of the increased respiratory rate; paralysis accompanied the return to normal of the O_2 consumption. 1441
  - (4) In marked contrast to DDT, DDD, methoxychlor, etc., a higher mortality in Musca domestica, treated with dieldrin, takes place at a holding temperature of 90°F than at 70°F. The same phenomenon is reported for Blattella. 1561, 1305
  - (5) Application of dieldrin to the leg of Periplaneta americana resulted in trains of repetitive discharges of relatively low voltage and frequency (compared with DDT) which were recorded from the crural nerve; the effect followed a latent period of ca 2 hours. 520
  - (6) The mechanism of toxic action of dieldrin is as yet obscure.
  - (7) Periplaneta americana coxal muscle cytochrome oxidase preparations showed complete inhibition of enzyme activity by dieldrin at 10^{-3}, 10^{-5} M concentrations; the onset of the effect was slow as with DDT, aldrin, chlordane, and in contrast with rapid onset in case of DDD, methoxychlor, lindane, toxaphene. 2305

b) Histopathological effects:
  - (1) When applied to the first abdominal pro-legs of Heliothis armigera larva the following effects were noted with dieldrin: 502
    - (a) Marked histological changes,
    - (b) Extrusion of hind gut through the anus,
    - (c) Degeneration of cells of the midgut epithelium, destruction of the peritrophic membrane, dense chromatin clumping in nuclei. The epithelium was not sloughed; muscles, basement membrane, remained virtually intact, with little or no degeneration,
    - (d) Dense chromatin clumping in nuclei of fat-body cells,
    - (e) Vacuolation, chromatin clumping, in the supporting muscularis of the hindgut,
    - (f) Slight degeneration of nuclei in cells of the Malpighian tubules, with an increase, in the lumen of the tubules, of a hematoxinophilic substance.
    - (g) No evidence of histopathological change in the nervous system.

c) Resistance to dieldrin has appeared by selection both in exposed "populations" of Musca domestica under field conditions and as a result of laboratory experimentation. 373, 2231, 353, 371
  - (1) Certain DDT-resistant strains show a concomitant increase in dieldrin resistance.
  - (2) Certain lindane "fast", or resistant strains show likewise a concomitant (or "cross") resistance to dieldrin.
  - (3) Consult, in this work the section titled Resistance and the table of insect toxicity values for dieldrin in this section.

57

DIETHYL 2-CHLOROVINYL PHOSPHATE
(Diethyl chlorovinyl phosphate; Compound 1836)



$$\begin{matrix} C_2H_5O \\ C_2H_5O \end{matrix}\!\!>\overset{O}{\overset{\|}{P}}-O-\overset{H}{\overset{|}{C}}=\overset{H}{\overset{|}{C}}-Cl$$

Molecular weight: 179.131

GENERAL

[Refs.: 599, 600, 2231, 2120, 2651, 2942]

A compound whose insecticidal and acaricidal properties have been recently reported (1953). Diethyl 2-chlorovinyl phosphate belongs to that general class of modern pesticides called the organic phosphate or "organophosphorus" insecticides. A general treatment may be consulted in this work. Furthermore, this compound has shown properties which place it among the systemic insecticides (consult the general treatment in this work under that title). Thus, when applied to a part of a plant, for example leaves, stems, roots, diethyl 2-chlorovinyl phosphate is rapidly absorbed into the plant tissues, and thence translocated to other not treated parts in amounts sufficient to exert there a toxic effect on insects or mites, in contact with, or feeding upon, the plant or its juices. It is, moreover, a systemic insecticide of the "endolytic" type. As such, diethyl 2-chlorovinyl phosphate exerts its toxic effect in the plant in its original state, not being transformed or metabolized, as is the case with "endometatoxic" substances, by the plant into a second toxic product or group of metabolites upon which the insecticidal effect depends. As an "endolytic" systemic insecticide, diethyl 2-chlorovinyl phosphate exerts its effect until broken down by, or dissipated from, the treated plant by outward movement in the transpiration stream.

PHYSICAL, CHEMICAL

A colorless liquid; b.p. 116°C at 10 mm Hg; sparingly soluble (to the extent of 1%) in water; relatively stable in aqueous emulsions, and retaining activity for at least 7 days; markedly volatile, 38% per hour being lost from glass plates at room temperature.

TOXICOLOGICAL

1) Acute toxicity for higher animals

Animal	Route	Dose	Dosage (mg/k)	
Mouse ♂	or	LD_{50}	32.9 (31.1-34.9)	1837
Mouse ♀	or	LD_{50}	18.0 (15.3-21.2)	1837
Rat ♂	or	LD_{50}	10.0 (9.4-10.7)	1837
Rat ♀	or	LD_{50}	10.5 (9.9-11.1)	1837
Rat ☿	ip	LD_{50}	9.0 (7.4-11.3)	1837
Rabbit ♂	or	LD_{50}	3.4 (2.3- 4.5)	1837
Rabbit ♂	ct	LD_{50}	17.6 (8.0-27.2)	1837

a) Inhibits mammalian acetylcholine esterase; the ID_{50} (inhibitory dose giving 50% inhibition) being, for human erythrocyte acetylcholine esterase, 1.7×10^{-5} M.

2) Pharmacological, pharmacodynamical, physiological, etc.:
   a) Consult the general treatment of Organic Phosphates in this work.

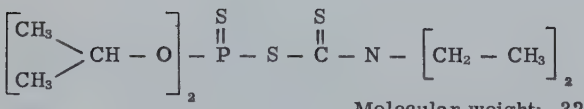
3) Phytotoxicity:
   a) No data; use as a systemic insecticide and acaricide would indicate a fair margin of safety for certain plants at least.
      (1) Consult the treatment in this work of the near analogue, dimethyl 2, 2-dichlorovinyl phosphate.

4) Toxicity for insects; acarines:
   a) The systemic acaricidal properties were tested at concentrations of 0.1%, 1.0% and comparison made with results obtained by use of 0.5% solutions. 599
      (1) Toxicity disappeared from the treated plants at the same relative rate with both the lower and higher dosages.
      (2) Definite acaricidal action was had at both concentrations.
      (3) The substance entered plants to the fullest extent in the early minutes after application.
      (4) No increase in toxic effect for a given dosage with longer exposure times was noted.
      (5) Moved out of plant with the transpiration stream. Vapors from plants treated by soil application killed phytophagous mites on untreated plants enclosed in the same battery jar with treated plants. The fumigant effect, with such transpiration vapors, endured for 24 hours after which effectiveness was lost.
      (6) The indications are those of a potent, but comparatively evanescent, systemic acaricidal action.

b) This compound (and its dimethyl analogue), being extremely toxic to insects, was tested against Musca domestica adults and Periplaneta americana adults and large nymphs for residual action. 1588
   (1) The vapor pressure and rate of disappearance from treated surfaces proved too high for success with the pure compound in solution.
   (2) Addition of chlorinated terphenyls, e.g. Araclor 5460, enhanced the residual action vs. Musca outstandingly when used in the proportion 1 to 4 (insecticide—terphenyl).
   (3) Combinations of diethyl 2-chlorovinyl phosphate with terphenyl, (1 to 4) yielded 100% mortality for Musca on residues 2, 4-5, 10, 30, 60 days old. The insecticide alone yielded 33% mortality on 2 hour residues, 2% on 4-5 day old residues, 0% on 10 day old residues. The dimethyl analogue used alone gave 50% kills on 2 hour old residues, 2% kills on 4-5, and 0% kills on 10 day old residues; with terphenyls 100% mortalities were registered on 2 hour, 4-5 day, 10, 30, 60 day old residues.
   (4) Vs. Periplaneta americana, for which the insecticide alone gave 0% kills on 2 hour old residues, insecticide—terphenyl (1 to 4) yielded 100% kills on 4-5 and 10 day old residues, 94% kills on 30 day and 100% kills on 60 day residues. The dimethyl analogue gave comparable results (0% kills on 4-5 day old insecticide (alone) residues, 100% on 4-5, 10, 60 day old terphenyl-insecticide residues and 97% kills on 30 day old terphenyl-insecticide residues.)
   (5) Using Tribolium confusum in tests, insecticide (alone) residues yielded 0% kills on 4-5 day old deposits; with insecticide-terphenyl (1 to 4) 100% kills were registered on 4-5 and 10 day old residues, 6% on 30 day old and 24% on 60 day old residues. The dimethyl analogue, which gave 0% kills on 4-5 day old insecticide (alone) deposits, yielded 100% kills on 4-5, 10, 30, 60 day old insecticide-terphenyl (1 to 4) deposits.
   (6) Application was at the rate of 100 mg per ft^2 terphenyl in all tests.

58

DIETHYLDITHIOCARBAMIC PHOSPHORODITHIOIC ANHYDROSULFIDE, O,O-DIISOPROPYL ESTER (Diethyldithiocarbamic anhydride of O,O-diisopropyl thionophosphoric acid; Holcomb Compound 326)



$$\left[\begin{matrix}CH_3\\CH_3\end{matrix}\!>CH-O\right]_2-\overset{S}{\overset{\|}{P}}-S-\overset{S}{\overset{\|}{C}}-N-\left[CH_2-CH_3\right]_2$$

Molecular weight: 329.483

GENERAL

[Refs.: 2032, 2120]

An experimental compound which has given evidence of effectiveness against all stages of Two-spotted, Atlantic and European red spider mites, and shown promise as an insecticide for melon, black, and pale-green chrysanthemum, potato, and several species of greenhouse aphids. Promise has been shown also against the clover and citrus red mites. A communication from the contributor [2032] states, "in December of 1954 we discontinued development of this material because of high raw material costs, and other considerations."

PHYSICAL, CHEMICAL

A yellow, oily liquid; at 130°C (at $<$1 mm Hg) decomposes; forms a glass at -70 to -80°C; insoluble in water, ethylene glycol; miscible with ethanol, xylene, acetone, cyclohexanone, benzene, Deobase, 2-propanol, diacetone alcohol, octanol, methyl isobutyl ketone, ethyl acetate, methyl naphthalene, toluene, cyclohexane, heptane, Nujol®, pyridine, dimethyl formamide, ethyl ether, isopropyl ether, ethyl cellosolve, chloroform, carbon disulfide; stable to light and heat up to 130°C; subject to alkaline hydrolysis; incompatible with lime-sulfur, Bordeaux mixture and other alkaline spray materials; compatible with DDT, BHC, chlordane, methoxychlor, lead arsenate, ferbam, nabam, captan, Manzate, wettable sulfur. Formulated experimentally as 25% wettable powders, 25% emulsifiable concentrates, dusts.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse (Swiss white)	or	LD_{50}	290	In propylene glycol.	2032
Mouse (Swiss white)	ip	LD_{50}	220	In propylene glycol.	2032

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse (Swiss white)	sc	LD_{50}	295	In propylene glycol.	2032
Rat (white)	or	LD_{50}	320	In propylene glycol.	2032

2) Subacute toxicity:

a) Rats, receiving 1/10th the acute oral dosage daily for 6 weeks, showed at autopsy no damage to heart, liver, kidneys. No symptoms of intoxication shown by human handlers, processors, appliers, *under adequate precautions*. 2032

3) Pharmacological, pharmacodynamic, etc.

a) Tests using isolated turtle heart strips and rabbit intestine, did not indicate inhibition of acetylcholine esterase. 2032

4) Phytotoxicity:

a) Applied at 2 lbs 25% wettable powder per 100 gallons gave no damage to foliage of: 2032

Corn
Bean
Tomato
Potato
Eggplant
Cucumber
Melon
Cabbage
Apple
Chrysanthemum
Caladium
African violet
Begonia
English ivy
Acalphia
Croton
Periwinkle
Salvia
Delphinium
Achyranthes
Pachysandra
Lantana
Ageratum
Buddleia
Coleus
Pansy
Geranium
Poinsettia
Isoloma
Petunia
Dahlia
Spruce
Yew
Pine
Hemlock
Fir
Arbor vitae
Elm
Maple

5) Toxicity to insects, acarines:

a) At 1-2 lbs (25% wettable powder) per 100 gallons yielded complete control of adults, nymphs of *Tetranychus bimaculatus*, Atlantic and European red spider mites. 2032

b) At 2 lbs (25% wettable powder) per 100 gallons gave 75%—100% control of eggs of *T. bimaculatus*, 85%—100% control of European red mite eggs. 2032

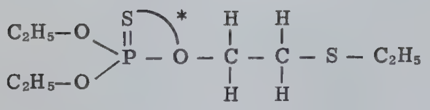
c) At 1-2 lbs (25% wettable powder) per 100 gallons showed complete control of melon, black and pale-green chrysanthemum, potato aphids (and several species of greenhouse aphids) with no appearance of nymphal colonies after 7 days. 2032

d) 2-2 1/2 lbs (25% wettable powder) or 1 qt emulsifiable concentrate per 100 gallons has been recommended, in a preliminary way, for field use against aphids, mites. 2032

59

O,O-DIETHYL-O-2-(ETHYLMERCAPTO)-ETHYL THIONOPHOSPHATE

(Systox ®; Demeton; O,O-Diethyl-O-2-ethylmercapto-ethyl phosphonothioate; Ethylmercaptoethyl diethyl thiophosphate; Diethoxythiophosphoric acid ester of 2-ethylmercaptoethanol; E-1059)



(= the thiono-isomer)
(* Interchange of S=, O= here → thiol-isomer.)

$C_8H_{19}O_3S_2P$

Molecular weight: 258.339

GENERAL

(Also consult Systemic Insecticides)
[Refs.: 3204, 353, 2231, 2120, 125, 2651, 1415, 2236, 1615, 17, 1072, 2256, 18, 2595, 2119, 1298, 2878, 2650, 1285, 89, 1825, 3304, 3181, 2942]

Systox®is a commercial product containing the above compound (for which Demeton has been accepted as a common name) as the active ingredient. One of that class of newer insecticides designated commonly as "organophosphorus" insecticides, or simply, as organic phosphate insecticides. Within this class, Demeton belongs to the category known as systemic insecticides, i.e,, materials having the property of entering the tissues and sap of plants, there to exert, on biting or sucking arthropods, a toxic effect per se, or as modified into other compounds by the action of the plant internal environment. Systox®, applied to plants as a spray, or watered on the soil, enters the plant, and is translocated upward therein. Systox® is an effective stomach and contact poison for insects and acarines, being particularly potent in action against aphids and phytophagous mites. Systox® is reported to spare insect predators of destructive plant pests, and to constitute, when properly used, no danger to Honeybees, and other pollinating insect forms. Possesses some fumigant action on mites and insects.

The presence of two isomers renders it somewhat difficult to make sharp precisions about Systox®, the commercial product. Of the two isomers present, the thiol-isomer is much the more potent insecticide and acaricide compared with the thiono-isomer. Moreover, the thiol-isomer is the more toxic to mammals. Nonetheless, the mixture of the two, in spite of the mediocre activity of the thiono-compound, constitutes an excellent and highly effective systemic insecticide to which the following insects and mites have been reported susceptible:

Aphis forbesi
Aphis gossypii
Aphis pomi
Anuraphis rosae
Brevicoryne brassicae
Eriosoma lanigerum
Macrosiphoniella sanborni
Macrosiphum pisi
Macrosiphum solanifolii
Macrosiphum rosae
Phorodon humuli

Toxoptera graminum
Paratetranychus pilosus
Paratetranychus citri
Tetranychus bimaculatus
Tetranychus atlanticus
Petrobia latens
Bryobia praetiosa
Rhizoglyphus echinopus
Epilachna varivestis (larva)
Epitrix hirtipennis

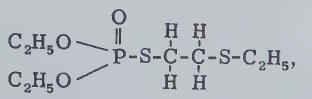
Attention is drawn to the sections in this work titled Organic Phosphates, and Systemic Insecticides for comparative data and data concerning properties general or common to these classes of insecticides and acaricides.

PHYSICAL, CHEMICAL

1) By the American licensee, Systox® is ascribed the following properties, presumably as the technical active ingredient: A light brown to pale yellow oily liquid of characteristic odor; b.p. 134°C at 2 mm Hg; v.p. 0.001 mm Hg at 33°C; $d_{4°}^{20°}$ 1.1183; $n_D^{20°}$ 1.4875; soluble in water to ca 0.01%, soluble in most organic solvents; as vapor 3.5 mg/m³ at 20°C. 3204
   a) Formulation: As a spray concentrate, containing the equivalent of 2 lbs active ingredient (Demeton) per gallon. 2651

2) To the thiono-isomer (see formula above) the following properties are ascribed: (pure) a colorless liquid of faint odor; b.p. 123°C at 1 mm Hg; $d_{4°}^{21°}$ 1.119; $n_D^{18°}$ 1.49; v.p. 5×10^{-4} mm Hg at 20°C; soluble in water to from 0.002-0.02%. 2773, 1468, 2651, 1074

3) Systox® isomerizes to form:



$$\begin{array}{l} C_2H_5O \\ C_2H_5O \end{array} \!\!> \overset{\overset{\displaystyle O}{\|}}{P}\text{-}S\text{-}\underset{H}{\overset{H}{C}}\text{-}\underset{H}{\overset{H}{C}}\text{-}S\text{-}C_2H_5,$$

O,O- diethyl-S-2-(ethylmercapto)-ethyl thiophosphate, the thiol-isomer, with 70% isomerization at 130°C, taking place in 3 hours. This isomer is ascribed the following properties: A colorless oil; b.p. 128°C at 1 mm Hg; $d_4^{21°}$ 1.132; $n_D^{18°}$ 1.5; soluble in water to from 0.02-2%.

4) The commercial product has a composition which approximates a 65:35 mixture of thiono- and thiol- compounds.

5) Thiono- and thiol- isomers undergo ready hydrolysis in alkaline media at the following rate constants (first order) at 25°C: Thiol-isomer K = 0.814 OH^- $min.^{-1}$; thiono-isomer K = 2.1 × 10^{-3} OH^- $min.^{-1}$. Both isomers can undergo acid hydrolysis at the following rate constants: Thiol-isomer K = 1.25 × 10^{-3} H^+ min^{-1} at 82.3°C; thiono-isomer K = 2.1 × 10^{-3} H^+ $min.^{-1}$ at 84.5°C.

6) Systox® is of dubious compatibility with zinc arsenate, organic mercurials, cryolite, Paris green, calcium arsenate. Incompatible with Bordeaux mixture, lime-sulfur, lime. Compatible with lead arsenate, nicotine sulfate, dieldrin, chlordane, aldrin, toxaphene, BHC, DDT, rotenone, pyrethrins, summer and dormant oils, fixed copper compounds, wettable sulfur, quinones. Emulsifiable concentrates (50% or less) form clear, colloidal solutions in all proportions with water. In 50% concentration on activated charcoal suitable for seed and soil treatment.

TOXICOLOGICAL

1) General: Highly toxic by ingestion, by skin absorption, by inhalation, and by way of the eye. Chronic exposure to sub-fatal amounts lowers the blood cholinesterase level, an effect reversible upon cessation of exposure. All precautions, viz. rubber gloves, protective clothing, goggles, respirator, to be taken during application. Immediate soap and warm water washing should follow any accidental contamination, and should be regularly practiced after any application procedure, and before eating or smoking. Contaminated clothing should be at once changed and not worn again before being washed. Application on very hot days, or in confined spaces, is to be avoided. Obviously, contact of Systox® with food is to be guarded against. 89 3204

2) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	inj	LD_{50}	> 20	The thiono-isomer.	2651
Mouse	inj	LD_{50}	< 2	The thiol-isomer.	2651
Rat ♀	or	LD_{50}	4	Isomer mixture as Systox®	188
Rat ♂	or	LD_{50}	10	As Systox®; ID_{50} ChE plasma, rat, 2.4×10^{-6} M brain, rat, 4×10^{-6} M	188
Rat	or	LD_{50}	ca 9		3204
Rat ♀	or	LD_{80}	9.4		2120
Rat	or	LD_{50}	9.4	As Systox®, technical.	2231
Rat	or	LD_{50}	7.5	The thiono-isomer.	2231
Rat	or	LD_{50}	1.5	The thiol-isomer.	2231
Rat	or	ca LD_{50}	6-12		129
Rat	ip	LD_{50}	3		861
Rat	inh	LC	ca 0.004 mg/1	2 hours exposure.	3204
Rabbit	ct	LD_{50}	24	Single inunction.	2120, 2231
Man	or	Acute	10-20 mg	Estimated acute dose.	89

a) Via the skin: somewhat more toxic than parathion; absorption swifter. By inhalation: Ca equitoxic with parathion. (See below for toxicity of oxidation derivatives of Systox® isomers for mouse.) 3204 89

3) Sub-acute, chronic toxicity, higher animals:

a) Severe hazard exists at the point of manufacture, formulation and application in absence of rigid precautions. 188

b) ♀ Rats: At 50 ppm in diet gave marked toxicity; no pathological changes. 188
At 20 ppm in diet yielded no gross or histopathological effects; at 16 weeks of exposure brain, blood, choline esterase activity were severely reduced.

c) Rats: 60 doses, 2 mg/k, oral, by tube over 90 days gave no growth rate decline. 2120

d) Rats: ♂♂ for 90 days at 10, 25 ppm in diet gave slight decline in plasma choline esterase activity; erythrocyte Ch E 68% of normal at 10 ppm; 57% at 25 ppm. 1461 3204
♂♂ for 90 days at 50, 100 ppm in diet showed plasma Ch E 68% of normal at 50 ppm; 73% at 100 ppm; erythrocyte Ch E 53% of normal at 50 ppm; 45% at 100 ppm; considerable mortality.

e) Rats: At 10 ppm showed normal growth, no adverse signs; at 50 ppm growth was depressed; gross effects. 188

ppm in diet	Ch E activity (% of Normal)			
	Brain	Plasma	Red Cell	Pathological Change
1	93	95.5	83	none
3	66	70	80	none
10	20	26.8	15.8	none

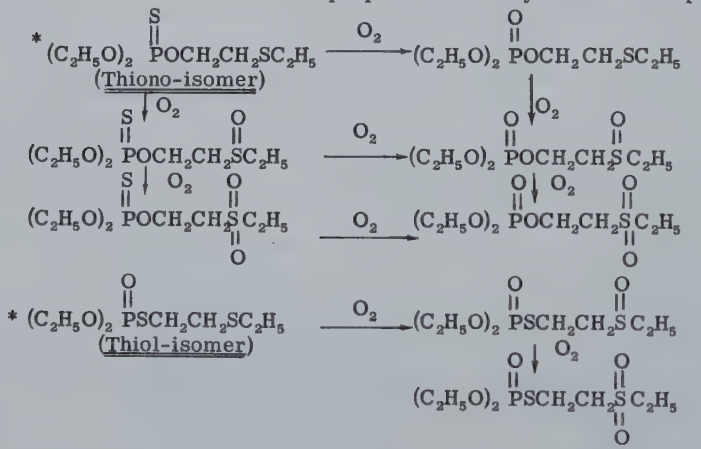
f) Rats: At 10, 20 ppm 3 months continuous feeding showed no deaths; decline in brain, blood Ch E; full recovery after withdrawal of Systox®.
g) Rats: 1/5 LD_{50} on each of 60 days in 90 days yielded no gross or microscopic pathology. 3204
h) Rabbits: For 4 months, on diet of clover, alfalfa, harvested 21 days after Systox® at 6 oz (active)/acre 3204
showed no adverse signs; no blood Ch E decline.

4) Residues; residue hazards:
a) Food crops not to be harvested prior to 15-21 days following last Systox® treatment. 129
b) Entry to, translocation in, plant is rapid, detoxification steady; at 6 oz (active)/acre residue level of <1 3204
ppm achieved within 21 days; residues may persist longer in oily, waxy substances, e.g. citrus peel com- 1298
ponents. Seed treatment, tree injection, soil application gave longer residual presence than foliage spraying; in soil residues drop to <1 ppm in 4-6 weeks. For Systox® residues in treated plants see Ref. 2238.
c) Cotton, treated at flowering with S^{35} tagged Systox®, produced seeds measurably radioactive 35 days later. 17

5) Pharmacological, pharmacodynamical, physiological, etc.:
a) Potent in vitro inhibition of animal Ch E; ID_{50}, human plasma Ch E = 8×10^{-6} M. 3204
b) Toxic action and symptoms characteristically those of cholinergic intoxication.
c) See, in this work, the section Organic Phosphates. For the metabolism of Systox® in the mouse consult Ref. 2237.

6) Phytotoxicity:
a) At recommended doses the hazard is slight. "Pink" and "petal fall" applications to apple trees (variety 2120
McIntosh) to be avoided. Phytotoxicity for young foliage of the walnut tree has been reported. Phytotox- 129, 2256
icity for peanut plant reported. Used as a field spray on corn, in concentration of 0.4 lb/100 gallon showed 1615
serious phytotoxicity: Stunting, delayed tasselling, unhealthy and undeveloped ears, with only 12-15% of plants producing healthy ears. Phytotoxic to corn as a soil soak, killing the plant in 3 weeks at 500 mg/plant, and producing banded chlorosis at 50 mg/plant. At 10 mg/cc, used as a seed soak, germination is delayed; at higher concentrations, as a seed soak (18 hrs. treatment), banded chlorosis develops in plants
from treated seeds. 3181

7) Toxicity for insects: Acarina:
a) General:
(1) As a systemic insecticide and acaricide, consideration of the toxicity of Systox® is inseparable from 1415
consideration of its activity and fate within the treated plant.
(2) Systox® is classed as an endometatoxic insecticide-acaricide, being converted in the living plant to 2651, 1072
secondary toxic substances which are toxic to insects, mites, higher animals. The following scheme 2231
of transformations has been proposed for the Systox® isomer pair: 3092, 1073



$$^{*}(C_2H_5O)_2\overset{S}{\overset{\|}{P}}OCH_2CH_2SC_2H_5 \xrightarrow{O_2} (C_2H_5O)_2\overset{O}{\overset{\|}{P}}OCH_2CH_2SC_2H_5$$

$$(C_2H_5O)_2\overset{S}{\overset{\|}{P}}OCH_2CH_2\overset{O}{\overset{\|}{S}}C_2H_5 \xrightarrow{O_2} (C_2H_5O)_2\overset{O}{\overset{\|}{P}}OCH_2CH_2\overset{O}{\overset{\|}{S}}C_2H_5$$

$$(C_2H_5O)_2\overset{S}{\overset{\|}{P}}OCH_2CH_2\underset{O}{\underset{\|}{\overset{O}{\overset{\|}{S}}}}C_2H_5 \xrightarrow{O_2} (C_2H_5O)_2\overset{O}{\overset{\|}{P}}OCH_2CH_2\underset{O}{\underset{\|}{\overset{O}{\overset{\|}{S}}}}C_2H_5$$

$$^{*}(C_2H_5O)_2\overset{O}{\overset{\|}{P}}SCH_2CH_2SC_2H_5 \xrightarrow{O_2} (C_2H_5O)_2\overset{O}{\overset{\|}{P}}SCH_2CH_2\overset{O}{\overset{\|}{S}}C_2H_5 \xrightarrow{O_2} (C_2H_5O)_2\overset{O}{\overset{\|}{P}}SCH_2CH_2\underset{O}{\underset{\|}{\overset{O}{\overset{\|}{S}}}}C_2H_5$$

(* = Systox® isomer pair)

Synthesis and tests of these products have shown properties in agreement with those of natural metabolites. The final breakdown of the toxic metabolites leads to diethylphosphoric acids and thiolalcohols which are toxicologically inactive. The thiol-isomer and/or its metabolites may escape from the plant as a vapor.

(3) Toxicity for insects, acarines, mice of oxidation derivatives of Systox® isomer pair. (Pure thiono- 1072, 2236
isomer has low activity as fly brain Ch E inhibitor, but the thiol-isomer is highly inhibitory of fly brain Ch E, as are the chief metabolites of both).

Derivative	LD_{50}		LC_{50} (% Concentration)	
	Mouse (ip, mg/k)	Musca (Topical, μg/fly)	Paratetranychus citri	Heliothrips haemorrhoidalis
O,O-Diethyl—:				
O-ethyl-2-sulfinylethyl phosphate	350	8.7	>0.1	0.1
O-ethyl-2-sulfonylethyl phosphate	27	3.7	.04	.3
O-ethyl-2-sulfinylethyl phosphorothionate	75	2.0	.04	.028
O-ethyl-2-sulfonylethyl phosphorothionate	75	1.2	.05	.002
O-ethyl-2-mercaptoethyl phosphate	20	0.74	.1	.038
S-ethyl-2-sulfinylethyl phosphorothiolate *	12	0.75	.0013	.0023 *
S-ethyl-2-sulfonylethyl phosphorothiolate *	10-15	1.2	.0014	.0028 *

*Probable principal toxic metabolites of the Systox® isomer pair. The major metabolite in the cotton plant 1073 of the thiol-isomer of Systox® 4-6 days after application was shown to be O, O-diethyl S-ethyl-2-sulfinylethyl phosphorothiolate (thiol-isomer sulfoxide) subsequently oxidized at a slower rate to O, O-diethyl S-ethylsulfonylethyl phosphorothiolate (thiol-isomer sulfone).

(4) As a contact insecticide for Paratetranychus citri, Heliothrips haemorrhoidalis, the thiol-isomer of Systox® is 3-5 times as toxic as the thiono-isomer. 2236 1468

(a) A similar difference in toxicity characterises the metabolites of the thiono- and thiol-isomers in the living plant.

$$\text{LD}_{100} \text{ for P. citri, H. haemorrhoidalis } \begin{cases} \text{thiono-isomer metabolite} = \text{ca } 300\ \mu\text{g/g lemon leaf (ca 300 ppm)} \\ \text{thiol-isomer metabolite} = <\ 40\ \mu\text{g/g lemon leaf (ca 40 ppm)} \end{cases}$$

(b) The thiono-isomer is a weaker in vitro inhibitor of human plasma Ch E than the thiol-isomer.

$$\text{ID}_{50} \text{ for human plasma Ch E } \begin{cases} \text{thiono-isomer} = 1 \times 10^{-5}\ \text{M} \\ \text{thiol - isomer} = 3 \times 10^{-6}\ \text{M} \end{cases}$$

(c) Preparations of S^{35} and P^{32} marked thiono- and thiol- isomers showed the following comparative behavior in bean, lemon, plants:
Both isomers are absorbed by roots and stems of lemon and translocated to the leaves in amounts toxic for Paratetranychus citri, Heliothrips haemorrhoidalis. Applied to bean and lemon stems, the thiol-isomer accumulated in upper leaves 5-10 times faster than the thiono-isomer and was responsible for the major part of the systemic toxic action on mites, thrips.

(d) Translocated materials concentrate more strongly in the peripheral growing areas and upper leaves of treated plants.

(e) Rapid metabolism of both isomers follows absorption and translocation; secondary toxicants are formed. 80-90% of the radioactivity due to S^{35}, P^{32} of bean leaves is in metabolites within 24 hrs. Metabolism to secondary toxicants somewhat slower in lemon plants, 97-100% of total radioactivity in metabolite form within 4 days. Three metabolites for each isomer have been chromatographically isolated. The LD_{50}, ip, for Mouse of the thiol-metabolites being 6-7, 10, ca. 10 mg/k respectively. A single toxic metabolite for each isomer constitutes 90% or more of the initial metabolic products of each.

(f) Bean plants, stem-treated with thiol-isomer of Systox®: Showed an appreciable amount in leaves in 2-4 hrs, which was rapidly converted, sequentially, to 2 metabolites, with one being predominant (95%), in 24 hrs, and responsible for the major part of systemic action.

(g) Radioactive vapors not isolated from leaves of bean, lemon, topically treated on the stems with S^{35}, P^{32}, marked isomers.

5) Entrance of thiono-, thiol- isomers of Systox® into lemon leaves dipped in 0.1% solutions, and via the lemon plant stem, topically treated with 20 microliters: 2231

Time (days)	Stem Treatment (lemon tree)				Leaf Dipping (lemon)	
	thiono-isomer		thiol-isomer		Time (hrs)	% of total thiono-isomer in leaf interior.
	ppm (upper leaves)	% metabolized	ppm (upper leaves)	% metabolized		
1	0	—	67	70.5	1	5.0
2	88	71	708	90.5	5-6	19.6
4-5	304	97	1740	100	24	14.7
					72	66.7

a) Distribution of thiono-isomer in various regions of lemon plant, stem treated: basal 23.5%, median 35.2%, terminal 41.3%.

b) Using P^{32} marked thiono-isomer, lemon plants, growing in solutions containing 0.0059% thiono-isomer, showed 210 ppm in leaf tissue in 4 wks, (root absorption).

6) Some results reported from the use of Systox® on plants vs. various pests: 2651

Plant	Pest	Experiment	Conc (%)	Treatment	Result	Country
Apple	Bryobia praetiosa	Field	0.012	Foliage Spray	100% kill after 24 days	USA
"	Tetranychus bimaculatus	"	0.012	"	" 20 "	"
"	Paratetranychus pilosus	"	0.016	"	" 16 "	"
Peach (seedling)	T. bimaculatus	Laboratory	0.04	"	" 12 "	"
Cherry	Myzus cerasi	Field	0.008	"	100% kill	"
Birch	Fenusa pusilla	"	0.031	"	100% kill after 16 days.	"
Holly	Phytomyza ilicis	"	0.06	"	Poor control(3.6% kill).	"
Juniper	Paratetranychus ununguis	"	0.04	"	96% kill after 5 days.	"
Fuchsia	Pseudococcus citri	Greenhouse	0.13	"	Good control.	"
Azalea	Paratetranychus ilicis	"	0.06	"	100% kill in 1 day.	"
Aster	Leafhoppers	Field	0.037	"	89% clean leaves.	"
Violet	T. bimaculatus	"	0.13	" (2×s)	100% kill after 35 days.	"
Pea	Macrosiphum pisi	"	0.025	"	Good control.	"
Cabbage	Brevicoryne brassicae	"	0.019	"	Excellent control.	"
Potato	Aphis many spp.	"	0.1	"	Very good control.	Great Britain.
Pea	M. pisi	"	500g/acre	Soil	Good control.	USA

Plant	Pest	Experiment	Conc (%)	Treatment	Result	Country
Cotton	*Septanychus texazona*	Laboratory	0.05	Foliage Spray	100% control.	USA
"	*Aphis gossypiella*	Field	0.2 lb/acre	Soil	Protection for 30 days.	Great Britain
Hop	*Phorodon humuli*	"	0.04	Foliage Spray	100% control.	Germany
Sugar beet	*Myzus persicae*	"	0.02	"	Excellent control.	Great Britain
Sugar beet	*Aphis fabae*	"	0.02	"	Excellent control.	Great Britain

7) Systox® on cotton plant:
   a) Translocation of Systox® in the cotton plant is reported to take place via the xylem only; movement is simultaneously upward and downward in the plant, with the upward movement more rapid. Seed, collected from plants treated at flowering with S^{35} marked Systox®, yielded measurable radioactivity 35 days after treatment. 17

8) Effect of Systox® on predators of *Aphis gossypii*, the cotton aphid, fed on poisoned aphids: Aphids poisoned by systemic action of treated plants or by direct contact: 16, 18
   a) 3 syrphids, *Baccha clavata*, *Metasyrphis wiedemannii*, *Allograpta obliqua*, are highly susceptible to Systox® poisoned aphids in all larval stages.
   b) 5 coccinellids ranged from 100% susceptible (*Scymnus haemorrhous*) to 3.7% susceptible (*Coleomegilla maculata*) with *S. creparus*, *Hippodamia convergens*, *Cycloneda sanguinea* larvae intermediate.
   c) Larval *Chrysopa rufilabris*, *C. oculata* proved virtually immune to Systox® in the form of Systox®- poisoned aphids.
   d) *Sphaerophoria flavicauda*, *Leucopis puncticornis* larvae proved susceptible to aphids poisoned by Systox® both with and without external contact.
   e) In the case of coccinellids, method of application of Systox® to the fed aphids proved important: Aphids having had external contact with Systox® were extremely poisonous to adults and larvae (100% kill) which were moribund 24 hrs. after feeding (*Coccinella undecempunctata*, *Scymnus syriacus*,). Aphids poisoned without external contact with Systox® affected only 2% of adults and no more than 27.8% of larvae of *Coccinella undecempunctata*; larvae of *Chrysopa vulgaris* proved virtually immune to poisoned aphids of either group.

9) Toxicity of Systox® for *Apis mellifera*; comparative, with certain other insecticides: 1718
   a) Qualitative: order of effectiveness as stomach, contact poisons:
      Parathion > TEPP > lindane > dieldrin > aldrin > chlordane > Systox® > BFPO > toxaphene
      (As Residual Films)
      Dieldrin > aldrin > lindane > parathion > chlordane > Systox®; others no measurable effect.
      (As Fumigants)
      Dieldrin > lindane > aldrin > parathion > chlordane; Systox®, others no measurable effect.
   b) Quantitative:

Material	Oral, In 50% Sugar Solution; µg/Bee for Mortality (24 Hrs) Of		
	20%	50%	90%
Systox®	1.256	1.478	1.884
Parathion	.018	.040	.144
TEPP	.052	.065	.093
Lindane	.026	.079	.346
Dieldrin	.223	.269	.354
Aldrin	.181	.239	.365
Chlordane	.831	1.122	1.730
Dimefox	1.25	1.90	3.506
Toxaphene	25.12	39.81	80.17

Material	As Contact Sprays; µg/cm^{2} To Give Mortality Of		
	20%	50%	90%
Systox®	4.32	5.12	6.62
Parathion	.257	.354	.574
TEPP	.358	.445	.621
Dieldrin	.386	.575	1.052
Aldrin	.327	.562	1.274
Lindane	.772	.851	.986
Chlordane	3.80	5.0	7.58
Dimefox	16.52	23.17	38.64
Toxaphene	36.73	44.67	59.98

Material	Contact, 1 hr, With Residual Films (Dry)				Vapors From Residual Dry Films	
	% Kill in 24 Hrs.	mg/cm^{2}	Av. Dose in Field	Oz/Acre	% Kill in 24 Hrs.	(µg/cm^{2})
Systox®	50	.01	—	—	0	18.5
Systox®	22	.0068	—	—	—	—
Dieldrin	90	.00009	.0014	2	100	.280
Dieldrin	10	.00004	—	—	0	.074

b) Quantitative:

Material	Contact, 1 hr, With Residual Films (Dry)				Vapors From Residual Dry Films	
	%Kill in 24 Hrs.	mg/cm²	Av. Dose in Field	Oz/Acre	% Kill in 24 Hrs.	(µg/cm²)
Aldrin	75	.00009	.0014	2	100	.74
Aldrin	0	.00004	—	—	0	.074
Lindane	100	.000280	.0028	4	100	.44
Lindane	0	.000074	—	—	0	.28
Parathion	90	.00054	.0014	2	100	5.0
Parathion	10	.00018	—	—	0	2.8
Chlordane	100	.0034	.0012	16	100	3.7
Chlordane	12	.0009	—	—	0	.37
TEPP	8	.00022	.0056	8	0	5.5
Toxaphene	9	.11	.0168	24	0	70.0
Toxaphene	0	.04	—	—	—	—
Dimefox	0	.05	—	—	0	74.0

10) Toxicity of Demeton (Systox®) for developmental stages of Tetranychus bimaculatus; mites placed on bean leaves treated in settling tower by method of Ebeling and Pence. 905
E = emulsifiable concentrate, W = wettable powder:

Compound	LC$_{50}$ (mg/100cc) 48 Hrs After Treatment			
	Adult	Larva	Egg	Adult On Leaf Surface Opposite Treated Surface
Demeton (Systox®) E	2.2	2.8	97	3
Diazinon W	12	28	180	115
EPN E	2.5	4.7	230	42
EPN W	4.8	7.7	460	76
Malathion E	2.5	7.3	320	84
Malathion W	4.2	11.5	840	125
Parathion E	5.6	13	190	21
Parathion W	4.5	10	370	27

11) Systox® (Demeton), and certain other compounds vs. Metatetranychus ulmi on apple trees (var. Northern Spy); New York, season of 1952: 1990

Compound	Dosage/ 100 gal.	% Reduction In Mites On Days After July 4 Spray		
		3 days	10 days	17 days
Systox® (Demeton) (42% liquid)	2 oz	98.5	100	100
Systox® (Demeton) (42% liquid)	4 oz	99.1	100	99.99
O,O-Diethyl-O-(2-isopropyl-4-methylpyrimidyl(6)thiophosphate(25% emuls.)	1 teaspoon	95.6	94.6	89.5
O,O-Diethyl-O-5(3-methylpyrazolyl)thiophosphate(25% emuls.)	1 pint	96.2	99.8	99.8
Diethyl-5-(3-methylpyrazolyl) phosphate (25% emuls.)	1 pint	95.3	98.8	98.6
Malathion (25% wettable powder)	2 lbs	97.2	99.6	98.6
Parathion (15% wettable powder)	1 lb	98.7	99.8	99.5
Malathion (50% emuls.)	1 pint	96.5	98.7	96.9
Tetra-n-propyl dithionopyrophosphate	2 lbs	99.3	98.5	97.3

12) Order of effectiveness Demeton (Systox®) and other compounds vs. Petrobia latens on dryland wheat in lbs/acre. Based on counts made 5 days and 2 weeks after treatment. Demeton 0.5 > parathion 0.5 > parathion 0.25 = demeton 0.25 > Metacide 0.25-0.5 = Schradan 0.5 > NPD 0.5-1.0 > chlorobenzilate 0.5 = Aramite® 0.33-0.66 = Ovotran®0.5-1.0 = compound 923 1.0-2.0 > TEPP 0.25-0.5 = EPN 0.5 = Malathion 0.75-1.5 = R-242 1.0-2.0 = Toxaphene 3.0 = compound 876 0.5 = Endrin 0.15-0.3 = DMC 0.25-0.5 > BHC 0.5-1.0. 1482

13) Other reports of insecticidal and acaricidal effectiveness of Systox®:

a) Peas, treated by soil, seed, foliage spray, or combination seed-spray methods: gave high control of Macrosiphum pisi (severe infestation conditions); seed germination and growth unaffected. Applied to seed and soil showed effective control through 80 days from planting to harvest. Less effective control by foliage spray of previously untreated plants 40 days after planting. Residue in soil treated peas = 1.6 ppm. Prolonged protection of pea plants of different degrees of maturity with a single dose of Demeton not achieved. 125 107

b) Eggplant, on soils treated prior to transplanting: Protected from Epitrix cucumeris, E. fuscula, Gargraphia solani; yield 2-4 times that of plants on untreated soils. 125

c) On Alfalfa vs. Macrosiphum pisi: At 0.25 lb/acre proved most effective of 8 types of treatment. 0.5 - 1 lb/acre on mature alfalfa gave virtual eradication of M.pisi for 2 weeks. 718 2595

d) Vs. Brevicoryne brassicae at 0.19, 0.38 lb/acre gave > 90% control for 8 days; watering of seedling cabbage before transplanting led to excellent control for 2 months; sprays at 0.5-2.0 lb/acre gave control for 50 days; applied as solution to base of cabbage plants newly set gave control until harvest. 3282 2595

e) Vs. Rhopalosiphum pseudobrassicae (on turnip): At 0.19, 0.38 lb per acre gave control lasting 2 weeks. 838

f) Vs. Paratetranychus pratensis on wheat: Systox®(and Parathion) gave best control of all the acaricides tested. 1442

g) Vs. Chromaphis juglandicola (including the parathion-resistant strain): Systox® gave complete control. (see Phytotoxicity) 2256

h) Vs. Tetranychus atlanticus: Outstanding control at 0.5, 1.0 lb per acre; superior to OMPA at 2 lb per acre. 2595

i) Vs. Anuraphis tulipae (on carrot): Fair to good control at 1.4 lbs per acre; fair control at 0.5 lb per acre. 2595

j) Vs. Myzus persicae (on sugar beet): Excellent control at 0.55-1.4 lb per acre. 2595

k) Vs. Thrips tabaci: No control. 2595

l) Vs. Tarsonemus pallidus (on strawberry): No control at 1, 2 lbs per acre. 2595

m) Vs. Meloidogyne hapla (nematode), Frankliniella fusca (thrip), Empoasca fabae (fleahopper) Diabrotica undecimpunctata (corn rootworm) as soil drench for peanuts: 1615
   (1) Significant systemic control of thrips at 4.2 lb or more per acre.
   (2) Significant systemic control of leafhopper at 1 lb per acre.
   (3) Effective control of either thrips or leafhoppers required 16.8 lbs per acre, at which rate 72% control of Diabrotica was obtained. Nematodes were significantly reduced at 2.1 lb per acre; effective control only at 16.8 lbs per acre. Phytotoxicity (spot necrosis of leaves) grew progressively severe with increasing dosages.

n) Vs. Myzus persicae: Recent data, see Refs.: 1825, 3304.

o) Vs. Tetranychus telarius: Recent data, see Refs.: 1825, 3304.

14) For screening test data vs Lice, mosquito larvae, flies see Ref. 1801.

15) Systox® (Demeton) effects on beneficial insects and arthropod "populations":

a) Dangerous to Typhlodromus (mite predaceous on other mites), with consequent enhancement of red spider "populations" noted after application. 2650

b) Systox®, and meta-Systox, kill high percentages of predators of Aphis fabae and Brevicoryne brassicae by contact and via poisoned prey. 2650

c) Toxicity of Demeton (Systox®) for Peregrinus maidis (corn leaf hopper) and its egg predator Cyrtorhinus mundulus: 3181

As contact spray; spray tower application by method of Ebeling:

P. maidis	LC_{50} 24 hrs: 0.044 (.041-.046) mg/cc	for fiducial limits P = 0.05
C. mundulus	LC_{50} 24 hrs: 0.037 (.031-.044) mg/cc	for fiducial limits P = 0.05

Mortality of P. maidis, on corn plants produced from seed treated for 18 hrs by soaking in various concentrations of Demeton before sowing:

Concentration (mg/cc)	% Kill Of P. maidis On Days After Treatment Shown				
	10 days	12 days	18 days	28 days	42 days
10.0	100	100	85	75	25
1.0	96	38	40	35	4
0.1	40	27	0	—	—
Control	0	0	0	8	0

Mortality of P. maidis and C. mundulus, on corn plants watered with Demeton solutions at various dosages per plant:

(Mg/Plant)	% Kill On Days After Treatment Shown							
	P. maidis						C. mundulus	
	2 days	7 days	14 days	21 days	26 days	40 days	1 day	7 days
500	100	100	100	100	plant dead		—	—
50	100	100	100	96	86	47	—	—
25	100	100	89	75	73	13	100	10
12.5	100	100	67	47	5	—	80	25
5.0	100	91	33	25	0	—	20	0
2.5	—	—	—	—	—	—	20	10
1.3	—	—	—	—	—	—	0	0
.5	14	5	0	0	0	—	—	—

(1) Demeton, by contact, is equally toxic to the pest P. maidis and the predator C. mundulus. Used as a soil soak Demeton exercised on the predator a potent toxic effect by fumigant action from the leaves of corn plants to which the insecticide was quickly translocated from the roots to all the aerial parts. Demeton affected the predator "population" almost as seriously as did DDT. By contrast, Schradan is 3 times as toxic for pest as for predator, although both Demeton and Schradan, applied as foliage sprays or soil soaks, are quickly translocated from the treated to the untreated corn plant parts. The translocation of Demeton is more rapid than the translocation of Schradan. Demeton is a highly effective seed treatment for corn, with regard to its action on P. maidis.

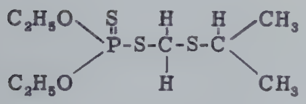
(2) A notable phytotoxicity of Demeton for corn, by all routes of application, is to be remarked. 500 mg per plant as a soil soak gave discoloration, stunting, severe "burning", drying up of foliage and death in 3 weeks. At 50 mg per plant, as a soil soak, banded chlorosis was produced. Field application at 0.4 lb per 100 gallons produced serious phytotoxicity for corn.

Addendum of recent data on Systox®:

1) Systemic action in plants of P^{32} labelled (radioactive) Systox thiol-isomer sulfoxide, and Systox thiol-isomer methosulfate: 2239
   - a) The thiol-isomer sulfoxide appears to establish itself more firmly as the principal toxic plant metabolite of Systox thiol-isomer.
     - (1) When applied to stems of young cotton plants, accumulation of radioactivity in the leaves was most rapid, using the thiol-isomer of Systox®, to a period of 14 days after application. Subsequently to 14 days, the thiol-isomer sulfoxide yielded the higher values.
     - (2) Using thiol-isomer methosulfate, accumulation of radioactivity in cotton plant leaves is much slower than in case of thiol-isomer, or thiol-isomer sulfoxide. This may indicate a low penetration capacity through the plant cuticulum.
   - b) Order of penetration and spread through the young lemon leaf interior: Thiol-isomer methosulfate $<$ thiol-isomer sulfoxide $<$ thiono-isomer $<$ thiol-isomer.
   - c) Rates of metabolism and decomposition in the plant interior of the thiol-isomer and thiol-isomer sulfoxide are approximately equal; in either case, small amounts of thiol-isomer sulfone appear.

60

O,O-DIETHYL-S-2-ISOPROPYLMERCAPTOMETHYL DITHIOPHOSPHATE (TM 12008)



Molecular weight: 254.405

GENERAL

Experimental insecticide and acaricide which has shown excellent contact and systemic action against certain insects and phytophagous mites. Also see TM 12009, TM 12013, in this work. 1660 2231

PHYSICAL, CHEMICAL

No data available to this compilation.

TOXICOLOGICAL

1) Toxicity for higher animals:
   - a) Stated to be 5-10 times as toxic to mammals as parathion, q.v. 2231

2) Phytotoxicity:
   - a) No data available to this compilation.

3) Toxicity for insects and acarines:
   - a) Action of TM 12008 on certain cotton insects, when used as a seed application, at 4 lbs per 100 lbs of seed: 1660

Insect	% Mortality Of Insects On Plants At Stated Time After Seed Treatment					
	On Seedlings	On Plants Growing In Cans For			Field Plants; Cage Tests	
Time after seed treatment	1 wk	2 wks	3 wks	4 wks	5 wks	6 wks
Anthonomus grandis (adult)	100	100	72	63	11	0
" " toxaphene spray 2 lb/acre (control)	84	62	59	60	53	42
Alabama argillacea (newly hatched)	100	100	100	97	74	59

(1) At 3 weeks time after seed treatment plants were 100% toxic to: Aphis gossypii, Tetranychus desertorum, Psallus seriatus (adult), Bucculatrix thurberiella (larva, newly hatched), Estigmene acraea (larva), Frankliniella tritici. Not effective vs Heliothis armigera (larva, newly hatched). 1660

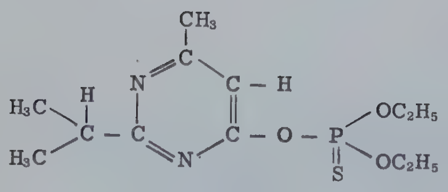
(2) The mode of systemic action is obvious in the effectiveness of the substance on foliage insects when used as a seed dressing. The substance is tentatively considered endometatoxic. 2231

4) *Addendum*: Parencia Jr., C. R., et al., The Journal of Economic Entomology *50 (1)*: 31, 1957*:
  a) TM 12008, and TM 12009, q.v., were employed, during the seasons 1954, 1955 (Waco, Texas), as seed treatments for systemic action vs. certain insects of cotton, viz., *Frankliniella* sp., *Aphis gossypii*, *Liriomyza pusilla*, *Psallus seriatus* and overwintered *Anthonomus grandis* in field experiments.
    (1) At 0.5 lb per acre in 1954 TM 12008 reduced plant emergence from treated seed by 13% (reduction by TM 12009 = 39%).
    (2) Effective control (1954) of *Frankliniella* sp. was had for 3.5 weeks with some control for an additional week after plant emergence. TM 12008 proved slightly superior to TM 12009. *Aphis gossypii* was controlled during 4.5 weeks.
    (3) In experiences of 1955, application at 1 lb per acre, TM 12008 did not give adverse effects on plant emergence and insect control results as follows were had:
      (a) *Liriomyza pusilla* failed to develop to any extent on cotyledons.
      (b) *Frankliniella* sp. was controlled for 5 weeks following plant emergence with fading of effect to approach control plants after 6 weeks.
    (4) Results are given for a compound named American Cyanamid Company 3911 (not treated in this compilation) as well and phytotoxicity, under certain conditions, of TM 12008, TM 12009, and American Cyanamid Company 3911 is discussed.

* Attention was drawn to this paper too late for its inclusion in the cumulative, alphabetic bibliography of the present work.

61

O,O-DIETHYL-O-(2-ISOPROPYL-6-METHYL-4-PYRIMIDYL) PHOSPHOROTHIOATE (Diazinon; G-24480; O,O-Diethyl O-2-isopropyl-4-methylpyrimidyl-(6)-thiophosphonate; Isopropylmethylpyrimidyl diethyl thiophosphate; O,2-Isopropyl-4-methylpyrimidyl-O,O-diethyl phosphorothioate.)



Molecular weight: 303.337

GENERAL

(Consult also the general treatment, in this work, titled Organic Phosphates) [Refs.: 1121, 2231, 2120, 369, 1092, 1123, 1384, 1317, 1387, 1012, 1588, 1252, 1285, 1315, 1385, 2733, 1712, 2862]

An insecticide of recent introduction, belonging to the general class of insect toxicants referred to as organic phosphates or "organophosphorus" insecticides and, more specifically, to the category of thiophosphonates which includes such potent insecticides as parathion, methyl parathion, Chlorthion®, Potasan®, pyrazinon, q.v. Diazinon has shown promise for the control of houseflies, including chlorinated hydrocarbon resistant biotypes and various stable flies in barns, milking sheds, pens, etc., as a spray and a sweet dry or liquid bait. Pirazinon is most closely related to Diazinon, being O,O-diethyl O-(2-n-propyl-6-methyl-4-pyrimidyl) phosphorothioate. Diazinon is an inhibitor of mammalian choline esterase(s) *in vivo* and *in vitro*. Diazinon is powerfully toxic for normal, DDT-R, Chlordane-R, *Blattella germanica* and, unlike the dimethyl carbamates of pyrimidine, is active against acarines and lice. Diazinon is much less toxic than parathion, and shows little tendency to accumulate in the animal body.

PHYSICAL, CHEMICAL [Refs.: 1384, 2231, 1315]

Pure: A colorless liquid; technical: A pale to dark brown liquid; b.p. 83°-84°C at 0.002 mm Hg; $d_{20°}$ 1.116-1.118; $n_D^{20°}$ 1.4978-1.4981; v.p. 1.4×10^{-4} mm Hg at 20°C; soluble (technical) in water to the extent of 0.004% at 22°C, readily soluble to miscible in most organic solvents, for example, miscible with alcohol, acetone, xylene, petroleum solvents; relatively stable in alkaline media; slow hydrolysis in neutral water and at acid pH.

Formulations: Experimentally formulated in a variety of ways, for example, dry and wet sweet baits; with adjuvants such as Araclor 5460 to enhance residual effectiveness of sprays; in water emulsions and acetone formulations at 0.5%-10% Diazinon with butoxypropylene glycols (0.5-30%) to enhance residual effectiveness; in molasses etc.; as wettable powders.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) If the usual precautionary measures, appropriate to use of organic phosphates, are followed, no hazard should be expected from Diazinon. 369

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	96 mm^3/k	Technical product.	1123
Mouse	or	LD_{50}	122.5	As wettable powder.	1123
Mouse	or	LD_{50}	ca 100		1384, 1121
Mouse	or	LD_{50}	82	As active ingredient; given as technical 85% active in corn oil.	369
Rat	or	LD_{50}	235 mm^3/k	Technical product.	1123
Rat	or	LD_{50}	712.5	As wettable powder.	1123
Rat	or	LD_{50}	ca 900		1121
Rat	or	LD_{50}	220-270		854
Rat	or	LD_{50}	100-150	Active ingredient in technical product 85% active; in corn oil.	369
Rat	or	LD_{50}	264.5	Active ingred. in 25% wett. powdr.; suspension in methyl cellulose.	369
Guinea Pig	or	LD_{50}	320 mm^3/k	Technical product.	1123
Rabbit	or	LD_{50}	130 mm^3/k	Technical product.	1123
Rabbit	ct	LD_{50}	>4000	Active ingred.; applied as wett. pwdr.; single dose dry or moist, to clipped skin.	369

   b) Dermal toxicity rabbit: Repeated daily doses of technical Diazinon (85% active ingredient) to clipped skin under rubber sleeve: Dosages 0.1, 0.3, 0.5, 1.0 cc/k gave absorption via the intact skin, with some deaths at each dosage level generally following 3-5 applications. 369

2) Subacute feeding experiences: 1610, 369
   a) Rats, receiving 100, 1000 ppm, technical Diazinon in diet, 4 wk exposure: Showed food consumption comparable for experimentals and controls; 1000 ppm group showed slight growth retardation; no gross evidence of toxicity; no gross pathology (autopsy). 369
      (1) At 100 ppm, erythrocyte choline esterase was significantly inhibited; at 1000 ppm erythrocyte and brain choline esterase(s) was significantly inhibited; plasma choline esterase levels, at 100 ppm, 1000 ppm were not statistically different from controls.

3) Chronic feeding experiences: 1610, 369
   a) Rats, receiving 10, 100, 1000 ppm, active Diazinon, as 25% wettable powder, in the diet for 72 wk. showed no toxic signs attributable to Diazinon. 369
   b) Dogs, receiving active Diazinon, as 25% wettable powder, at levels up to 6.5 mg/k/day revealed no gross toxic signs, although choline esterase activity showed inhibition; at 9.3 mg/k/day and higher, toxic signs, associated with choline esterase inhibition, were manifest. 369
      (1) No pathology at gross autopsy; no histopathological signs in liver, kidney, bone marrow, intestines, adrenals, bladder, gonads. 369
      (2) At 4.6 mg/kg/day: In 2 wks plasma Ch E at 36%, erythrocyte Ch E at 59% of normal; at 12 weeks complete Ch E inhibition (plasma and erythrocytes.). 369
      (3) At 9.3 mg/k/day active Diazinon, complete Ch E inhibition (plasma, erythrocytes) during 5th week, after 25 doses; loss of weight, decreased appetite, soft feces. After withdrawal signs of toxicity were reversed. Plasma and erythrocyte Ch E at 8% and 21% of normal respectively at end of 2nd week. At end of the 4th week plasma Ch E stood at 1%, erythrocyte Ch E at 2% of normal. After withdrawal of Diazinon rapid regeneration of Ch E activity to normal took place after 2 weeks. 369
      (4) No gross signs of toxicity in dogs until Ch E activity was at <10% of normal. 369

4) Pharmacological, pharmacodynamical, physiological, etc., higher animals: 369
- a) At LD_{50} oral dosages, gross, systemic toxicity follows technical Diazinon or the wettable powder.
  - (1) Symptoms are characteristic of choline esterase(s) inhibition and include: Depression, salivation, lachrymation, rapid respiration, tremors, diarrhoea.
  - (2) Gross pathology in fatal cases: Hemorrhages in lungs, kidneys; gastrointestinal irritation. Survivors, after one week showed no significant residual effects.
- b) Dermal application of technical Diazinon or wettable powder:
  - (1) Mild dermal irritation with erythema, atonia, desquamation.
  - (2) Gross signs in fatal cases characteristic of choline esterase inhibition.
  - (3) Pathology in fatal cases: Hemorrhage of lungs, gastrointestinal and peritoneal irritation; in survivors no characteristic pathology.
- c) Effects of Diazinon are typical of organic phosphates and thiophosphates with the expected symptoms of choline esterase inhibition which is confirmed by direct determination of plasma and erythrocyte Ch E levels in subjects of chronic feeding tests.

5) Tests of Diazinon, fed to mammals (Guinea Pigs), as a chemotherapeutic measure vs. parasitic fly grubs (Callitroga hominivorax): 2185
- a) At 10, 25 mg/k gave ca. 100% kill of grubs present at time of treatment; 10 mg/k was effective in prophylaxis for 1 week, no new grubs following doses of 25 mg/k.
- b) Diazinon in peanut oil, subcutaneous at 5-50 mg/k yielded 100% kills of grubs present at time of treatment, and of those appearing in the succeeding 2 weeks. No dosage was effective at 4 weeks after injection.
- c) Bayer L 13/59, O,O-dimethyl-2,2,2-trichloro-1-hydroxyethyl phosphonate, at 100 mg/k gave results comparable to the preceding; Bayer 21/199, at 25 mg/k oral proved completely ineffective.

6) Phytotoxicity:
- a) No specific data are available to this compilation; inference drawn from tests of Diazinon for acaricidal systemic action in bean plants after solution culture application indicates that at certain levels, at least, the compound is not phytotoxic for these plants. 1121

7) Toxicity for insects:
- a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Blattella germanica (adult ♀)	Topical	LD_{50}	0.33 μg/insect	Normal biotype.	1012
Blattella germanica (adult ♀)	Topical	LD_{50}	0.78 μg/insect	DDT-R biotype.	1012
Blattella germanica (adult ♀)	Topical	LD_{50}	0.4 μg/insect	Chlordane-R biotype.	1012
Musca domestica (adult)	Topical	LD_{50}	4.6 μg/g		2231
Musca domestica (Auburn, DDT-R)	Topical	LD_{50} 24 hr	0.06 (.05-.07) μg/fly	In acetone solution; strain 14 times as resistant as Orlando.	2110
Musca domestica (Auburn, DDT-R)	Topical	LD_{50} 24 hr	3.01 μg/g	" " "	2110
Musca domestica (Orlando, DDT non-R)	Topical	LD_{50} 24 hr	0.1 (.09-.11) μg/fly	In acetone; strain 14 times as susceptible to DDT as Auburn.	2110
Musca domestica (Orlando, DDT non-R)	Topical	LD_{50} 24 hr	6.15 μg/g	" " "	2110
Anopheles quadrimaculatus (4th instar)	Medium	LC_{100}	.01,.025,.05,0.1 ppm	36% and 20% kills at .005, .0025 ppm.	1766
Anopheles quadrimaculatus Anopheles crucians	Medium		.05; 0.1 lb/acre	Gave 97% kill in field tests; 79% at 0.025 lb/acre, 58% at 0.01 lb/acre, 53% at 0.001 lb/acre.	1766
Bovicola caprae Bovicola limbatus	Contact Dip		.025;.05;.005%	Gave 100% kills of lice on dipped goats at stated concentrations (%).	2862
Haematopinus eurysternus	Contact (Spot)		.05;.1;.25%	Gave 100% kills; effective 1-2 weeks.	2862
Haematopinus eurysternus	Contact (Spot)		.01%	Gave 95% kills; effective 1 week; as spot treatment.	2862
Eomenacanthus stramineus	Contact Dust		1%	Gave 100% kills on chickens; effective ca 2 weeks.	2862
Chrysops discalis (adult)	Topical	LD_{50} (est)	90 μg/fly		2707
Chrysops discalis (adult)	Topical	LD_{90}	360 μg/fly		2707
Tetranychus bimaculatus (adult)	Contact Deposit	LC_{50}	0.012 g/100 cc	On leaves previously treated in settling tower.	905
Tetranychus bimaculatus (larva)	Contact Deposit	LC_{50}	0.028 g/100 cc	" "	905
Tetranychus bimaculatus (egg)	Contact Deposit	LC_{50}	0.18 g/100 cc	" "	905
Tetranychus bimaculatus (adult)		LC_{50}	0.115 g/100 cc	For mites on leaf surface opposite treated surface.	905
Musca domestica (adult ♀)	Topical	LD_{50}	0.03-0.04 μg/fly	In acetone; laboratory strain.	1761
Musca domestica (adult ♀)	Topical	LD_{50}	0.11 μg/fly	In acetone; Exposed field strain J 74.	1761
Musca domestica (adult ♀)	Topical	LD_{50}	0.13 μg/fly	In acetone; Exposed field strain J 79.	1761
Musca domestica (adult ♀)	Topical	LD_{50}	0.17 μg/fly	In acetone; Exposed field strain Z 127.	1761
Musca domestica (adult ♀)	Topical	LD_{50}	0.09 μg/fly	In acetone; Exposed field strain Z 129.	1761
Musca domestica (adult ♀)	Topical	LD_{50}	0.3 μg/fly	In acetone; Exposed field strain Z 149.	1761
Musca domestica (adult ♀)	Topical	LD_{50}	0.5 μg/fly	In acetone; Exposed field strain Z 150.	1761
Musca domestica (adult ♀)	Topical	LD_{50}	0.13 μg/fly	In acetone; Exposed field strain F 151.	1761
Musca domestica (adult)	Topical	LD_{50} 24 hr	0.092 μg/fly	In acetone sol.; by measured drop test.	1981
Fannia canicularis ♂ (adult)	Topical	LD_{50} 24 hr	0.054 μg/fly	Av. wgt fly = 6.89 mg (♂); in acetone sol.	1981
Fannia canicularis ♀ (adult)	Topical	LD_{50} 24 hr	0.098 μg/fly	Av. wgt fly = 7.35 mg (♀); in acetone sol.	1981

8) Comparative Toxicity, Diazinon, others for various insects:
- a) Toxicity of Diazinon and other compounds in cage tests vs. Musca domestica (Orlando #1 strain, almost completely DDT-immune) as dry, sugar baits: 1092

Insecticide and % Concentration		% Mortality In					Toxicity As % Mortality At 16 hrs. Of 1% Sugar Baits	
		15 min	30 min	1 hr	16 hrs	24 hrs	14 days old	28 days old
Diazinon	5%	13	57	97	100	100		
	2%	12	40	77	100	100	100	100
	1%	15	45	69	100	100		
	0.5%	18	44	67	100	100		

a) Toxicity of Diazinon and other compounds in cage tests vs. Musca domestica (Orlando #1 strain, almost completely DDT-immune) as dry, sugar baits: 1092

Insecticide and % Concentration		% Mortality In					Toxicity As % Mortality At 16 hrs. Of 1% Sugar Baits	
		15 min	30 min	1 hr	16 hrs	24 hrs	14 days old	28 days old
Diazinon	0.1%	16	41	73	99	100		
Malathion	5%	11	51	79	100	100	100	100
Malathion	2%	16	56	81	100	100		
Malathion	1%	10	42	80	100	100		
Malathion	0.5%	8	46	83	100	100		
Malathion	0.1%	2	18	52	99	100		
Bayer L 13/59	5%	19	67	92	100	100	100	100
Bayer L 13/59	2%	22	55	76	100	100		
Bayer L 13/59	1%	16	59	92	100	100		
Bayer L 13/59	0.5%	6	22	57	100	100		
Bayer L 13/59	0.1%	0	1	25	99	100		

b) Diazinon and other compounds: Effectiveness as dry baits vs. natural Musca domestica infestations in 11 dairy barns; 100 g bait per application. Flies highly resistant to chlorinated hydrocarbons: 1092

Insecticide and % Concentration		Pretreatment Count of Flies	No. Applications.	% Initial Reduction (4 hr)	% Daily Reduction	
					Average	Range
Diazinon	1.0	184	15	97	98	94-99
Diazinon	.5	122	10	67	87	69-97
Diazinon	.5	160	13	98	83	65-95
Diazinon	.25	211	6	97	83	53-99
Malathion	1.0	245	13	—	93	81-98
Malathion	.5	410	8	99	98	94-99
Malathion	.5	190	7	99	95	85-98
Malathion	.25	164	8	27	78	58-92
L 13/59	1.0	212	15	97	98	93-100
L 13/59	.5	249	4	79	65	48-75
L 13/59	.5		6 (150g)	—	78	61-95
L 13/59	.5	176	5	90	97	96-99
		In 2 Poultry Houses				
Diazinon	1.0	159	15	97	83	49-98
Malathion	1.0	240	4	0	0	0
Malathion	1.0	439	5 (400g)	79	91	83-99
L 13/59	1.0	142	15	90	90	61-99

c) Diazinon and other insecticides: Effectiveness in barns vs. Musca domestica biotypes, DDT-R and probably DDT-Susceptible: 1384

Barn	Treatment	Date	Days of Control	
1	Diazinon 1%	6/17	72	Fly biotypes not apparently DDT-R
4	Diazinon 1%	7/1	21	
5	Diazinon 1% + methoxychlor 1%	7/29	24	
3	Pyrolan 1% + methoxychlor 1%	6/17	14	
3	Pyrolan 1% + methoxychlor 1%	7/8	17	
3	Pyrolan 1% + methoxychlor 1%	9/2	16	
2	Pyramat 2% + methoxychlor 1%	6/17	21	
4	Pyramat 1%	6/17	2	
2	Pyramat 1% + methoxychlor 1%	7/29	21	
9	Diazinon 1% + methoxychlor 1%	8/15	30	Fly biotypes DDT-R.
6	Pyrolan 1% + methoxychlor 1%	8/12	3	
7	Pyrolan 1% + methoxychlor 1%	8/12	17	
8	Pyrolan 1% + methoxychlor 1%	7/29	5	
8	Pyrolan 1% + methoxychlor 1%	8/12	6	

Tests of Diazinon in 21 barns for fly control, 8 formulations, gave control for average of 40-50 days; in 3 barns a single treatment gave season-long control. 1387

Excellent in fly control in horse and cow barns; control from 3-4 weeks to season-long. Excellent vs. DDT-R strains, giving control at height of fly season where lindane and methoxychlor failed. Residual action 10 weeks vs. DDT non-R, 4 weeks vs. DDT-R biotypes. 1384

d) Effect of Diazinon in rearing medium of *Musca domestica* (final larval instar): 3331

Insecticide	% Kill Larvae	% Producing		
		Normal Puparia	Abnormal Puparia	Adults
Diazinon 1 mg/g medium	39	0	60	0
DDT 1 mg/g medium	2	98	0	91
Control	0	100	0	92

In field tests, under conditions of heavy infestation and poor sanitation, a single application, at 1% concentration, yielded control for 35 days. No evidence of resistance in biotype exposed to treated surfaces for 97 days; sun-exposed surfaces lost effectiveness sooner than interior surfaces.

e) Effect of Diazinon and other compounds on larval *Musca domestica*; field experiences on caged accumulations of organic matter suitable for fly breeding: 2733

Insecticide	Average % Kill At Concentration Shown; Sprays					
	3%	2%	1 %	0.5%	0.25%	0.125%
Diazinon	—	—	100	100	100	98
Aldrin	—	100	100	99	90	—
Chlordane	—	100	100	100	96	—
Copper naphthenate	—	100	100	96	90	—
DDT	—	—	100	100	100	94
Dieldrin	—	—	100	100	100	99
Endrin	—	—	100	100	100	100
Heptachlor	—	—	100	100	100	100
Lindane	—	—	100	100	100	100
Malathion	—	—	100	100	97	81
Naphthalene	—	100	100	98	48	—
Parathion	—	—	100	100	100	100
Phenothiazine	—	—	100	100	100	61
Sodium arsenite	100	94	55	38	—	—
Sodium pentachlorophenate	—	—	100	100	92	81
DDD	100	100	74	68	—	—
Tetrachlorophenate	—	100	100	98	57	—
Thiourea	—	100	100	94	86	—
Toxaphene	—	—	100	100	100	96

f) Comparative toxicity, Diazinon and other compounds vs. *Musca domestica* (adult) Auburn DDT-R strain, Orlando DDT-non R strain (Auburn = 14 times as resistant as Orlando); Topical application in acetone: 2110

Insecticide	Auburn			Orlando		
	LD_{50} 24 hrs (μg/fly)	Fiducial 0.95% Limits	LD_{50} 24 hrs (μg/g)	LD_{50} 24 hrs (μg/fly)	Fiducial 0.95% Limits	LD_{50} 24 hrs (μg/g)
Diazinon	0.06	(0.05-0.07)	3.01	0.1	(0.09-0.11)	6.15
Chlordane	29	(12-57)	2791.3	42	(42-84)	3586.8
Heptachlor	13	(11-17)	855.79	11	(8.75-15)	955.68
Methoxychlor	2.33	(2.03-2.53)	135.18	1.93	(1.33-2.33)	127.49
Chlorthion	0.14	(0.1-0.2)	10.52	0.21	(0.19-0.25)	16.89
American Cyanamid 4124	0.03	(0.03-0.03)	2.75	0.02	(0.02-0.03)	1.73

g) Toxicity of Diazinon and other compounds for the DDT-R, Chlordane-R and normal, biotypes of *Blattella germanica*; Topical application; adult ♀ insects: 1012

Insecticide	LD_{50} (μg/insect) Normal	DDT-R		Chlordane-R	
		LD_{50}(μg/insect)	Degree Resistance	LD_{50}(μg/insect)	Degree Resistance
Diazinon	0.33	0.78	2.4	0.4	1.2
DDT	13.5	25.0	1.9	19.0	1.4
Chlordane	2.3	4.1	1.8	250.0	108.6
Dieldrin	0.5	0.62	1.2	34.0	68
Allethrin (synergized)	0.76	1.3	1.7	1.0	1.3

h) Aphicidal action of Diazinon and other insecticides: 1285

Insecticide	Insect	Concentration (%)	% Mortality After			
			24 hrs.	72 hrs.	120 hrs.	456 hrs.
Pyrazothion	*Aphis pomi*	0.02	98.2	99.7	99.4	100
Diazinon	"	.02	85.7	90.9	73	30
Pyrazoxon	"	.02	96.5	100	98.5	96
OMPA	"	.06	73.9	91	97.7	100
Pyrazothion	*Sapphaphis plantaginea*	.02	5	100	100	100
Diazinon	" "	.02	94.8	100	100	100

h) Aphicidal action of Diazinon and other insecticides: 1285

Insecticide	Insect	Concentration (%)	% Mortality After 24 hrs.	72 hrs.	120 hrs.	456 hrs.
Pyrazoxon	Sapphaphis plantaginea	.02	99.3	100	100	100
OMPA	" "	.06	—	—	—	—

Insecticide	Insect	Concentration (%)	72 hrs.	120 hrs.	240 hrs.	288 hrs.	360 hrs.	504 hrs.
Pyrazothion	Phylloxera vastatrix	.02	24	—	78	—	—	54
Diazinon	" "	.04	83	94	90	100	94	96
Pyrazoxon	" "	.04	82	90	76	82	86	61
Systox®	" "	.04	78	95	57	90	58	92
Control	" "		38	13	11	2	2	4
Isolan	" "	.008	25	—	47	—	—	49

i) Systemic action of Diazinon and other compounds vs. Tetranychus bimaculatus on bean plants, root-dipped in insecticides at given concentration in Knop's solution: 1121

Insecticide	Conc. (g/100 l)	"Population" At Start mobile*	resting*	egg*	4 Days Later mobile	resting	egg	6 Days Later mobile	resting	egg
Diazinon	10	18	12	19	9	4	23	13	0	30
"	20	17	24	9	4	8	28	9	0	29
Pyrazothion	10	21	6	24	14	1	36	16	0	40
"	20	19	11	14	15	0	15	8	0	26
Pyrazoxon	10	12	5	49	0	0	14	0	0	2
"	20	14	8	22	0	0	8	0	0	1
Systox®	10	20	0	12	0	0	12	0	0	6
"	20	14	4	34	0	0	34	0	0	26
OMPA	10	11	8	45	0	0	38	2	0	31
"	20	14	4	31	0	0	31	0	0	27
Control	—	27	13	18	48	26	121	156	29	203

* = Stage of life cycle.

j) Toxicity of Diazinon and other compounds for Chrysops discalis; topical application, adults: 2707

Insecticide	Estimated LD_{50} (μg/fly)	LD_{90} (μg/fly)
Diazinon	90	360
Lindane	4	35
Endrin	9	80
DDT	20	250
Dieldrin	20	950
Methoxychlor	30	90
Aldrin	40	170
Heptachlor	40	200
EPN	48	120
Isodrin	60	170
Chlordane	60	650
Chlorthion	65	420
3-Chloro-4-methylumbelliferone,O,O-diethyl thiophosphate	90	910
Q-137	120	400
Malathion	130	330
Toxaphene	180	480

k) Diazinon and other compounds vs. Anopheles quadrimaculatus (4th instar larva); laboratory tests using insecticide + acetone + water suspensions:

Insecticide	% Mortality 48 Hrs At 0.1 ppm	.05 ppm	.025 ppm	.01 ppm	.005 ppm	.0025 ppm	.001 ppm	.0005 ppm
Diazinon	100	100	100	100	36	20	—	—
Sulfotepp	100	100	100	100	100	100	74	34
Parathion	100	100	100	100	100	96	56	34
EPN	100	100	100	100	100	96	32	—
Methyl parathion	100	100	100	100	100	67	—	—
O,O-Dimethyl O-(2-chloro-4-nitrophenyl) thiophosphate	100	100	100	96	86	62	62	44
Malathion	100	100	96	80	80	60	40	24
Ethyl o-nitrophenyl thionobenzene phosphonate	100	100	100	100	70	80	4	—
Paraoxon	100	100	100	82	50	—	—	—

k) Diazinon and other compounds vs. Anopheles quadrimaculatus (4th instar larva); Laboratory tests using insecticide + acetone + water suspensions:

Insecticide	% Mortality 48 Hrs At							
	0.1 ppm	.05 ppm	.025 ppm	.01 ppm	.005 ppm	.0025 ppm	.001 ppm	.0005 ppm
O,O-Dimethyl O-(3-chloro-4-umbelliferone) thiophosphate	100	100	100	64	46	24	—	—
Chlorthion	100	100	88	76	44	—	—	—
Potasan	100	98	56	30	5	—	—	—
O,O-Diethyl O-piperonyl thiophosphate	100	94	58	26	—	—	—	—
NPD	94	—	62	30	—	—	—	—
DDT	—	—	—	100	94	49	24	—

l) Diazinon and other insecticides as wall sprays in animal barns for the control of Musca domestica. Sprays with, and without, sugar in the formulation. Insecticides = closely related organic phosphates. Laboratory Tests. 1712

(1) "Knockdown" and mortality of flies exposed to treated wooden panels:

Insecticide	Form	With (+) Without (-) 12% Sugar	% Killed Or Down After				
			Residues 6 wk old		Residues 13 wk old		
			2 hrs	4 hrs	2 hrs	4 hrs	20 hrs
Diazinon (1%)	Emulsion	+	41	62	4	5	34
"	"	-	10	30	1	9	59
"	Wett. pwdr.	+	4	48	0	0	12
"	"	-	1	1	0	0	1
Pirazinon (1%)	"	+	1	4	6	8	12
"	"	-	1	7	9	20	31
Chlorthion (1%)	"	+	0	0	0	1	9
"	"	-	0	2	0	0	2
Experimental 4124 (1%)	Emulsion	+	21	44	47	72	89
"	"	-	0	0	0	0	14
Bayer L 13/59 (1%)	Water Solution	+	38	67	54	84	96
"	"	-	6	14	1	2	6
Malathion (1%)	Emulsion	+	12	68	21	51	80
"	"	-	0	0	1	3	4
"	Wett. pwdr.	+	0	1	1	1	3
"	"	-	5	15	0	0	3

(2) Diazinon and other compounds as 17 week old baits for Musca domestica:

Insecticide	Form	% "Knockdown" After				
		1 hr	2 hrs	3 hrs	4 hrs	20 hrs
Diazinon (1%)	Emulsion	16	52	94	100	100
Pirazinon (1%)	Wett. pwdr.	4	5	9	12	64
*Bayer L 13/59 (1%)	Water soluble	31	85	94	100	100
Chlorthion (1%)	Wett. pwdr.	0	1	14	40	98
Experimental 4124 (1%)	Emulsion	18	61	84	93	100
Malathion (1%)	Emulsion	7	63	75	85	98
"	Wett. pwdr.	9	58	78	86	99

* = Dipterex

All the above toxicants, as wet or dry baits (wet baits with 0.4% toxicant, dry baits with 1% toxicant), used regularly at 2 times a week were effective in farm barns to control flies.

m) Diazinon and other compounds in fly control. Laboratory and Field Tests: 1915

Insecticide	% Killed or Down (Laboratory)			Field Results
	30 min.	1 hr.	24 hrs.	
Diazinon (1%)	23	36	96	Excellent
Dipterex (Bayer L 13/59) (.1%)	54.5	56.5	100	"
Malathion (1%)	43	56	93	"

9) Influence of Adjuvants on Effectiveness of Diazinon Residues:

a) Influence of butoxypolypropylene glycol on duration of effectiveness of Diazinon residues on plywood and paper surfaces vs. Musca domestica 4-6 day old adults. Mortality determined at end of 24 hr. period. BPG itself has no residual toxicity for Musca: 1252

	10% H_2O Emulsion At	Exposure (min)	Age of Residue (days)	Mortality (%)
Diazinon (alone) Plywood	50 mg/100 in^2	15	21	100
" " "	"	10	77	100
" " "	"	3	126	0
" + BPG* "	" + 0.5% BPG	—	126	99
" " "	" " "	—	203	72
" " "	" + 10% "	—	126	91
" " "	" " "	—	203	81
" " "	" + 30% "	—	126	79
" " "	" " "	—	203	96
" 1% acetone sol on Filter Paper	25 mg/100 in^2	—	> 1	Ineffective
" " " " " " "	" + 2.5-10% BPG	—	12	Definite residual action
" 1% acetone sol on Plywood	0.75 mg/100 in^2	—	Within 1 week.	Ineffective
" " " " " "	" + 5%, 10% BPG	—	>5 weeks.	Effective

b) Effect of chlorinated terphenyls (Araclor 5460) on residual effectiveness of Diazinon for various insects: 1588

(1) Chlorinated terphenyls (Araclor 5460) enhance the residual effectiveness of Diazinon, with the best effect being obtained at an insecticide: terphenyl ratio of 1 : 4.

	% Mortality At Stated Age Of Residue			
	2 hrs	4-5 days	10 days	30 days
Vs. Musca domestica (adult):				
Diazinon (alone)	100	12	—	6
" + Araclor 5460 (100 mg/ft^2)	—	—	—	100
Vs. Periplaneta americana (adult and large nymph):				
Diazinon (alone)	100	0	—	—
" + Araclor 5460 (100 mg/ft^2)	96	26	4	35
Vs. Tribolium confusum (adult):				
Diazinon (alone)	—	2	—	—
" + Araclor 5460 (100 mg/ft^2)	—	22	3	0

(1) Preliminary outdoor tests with Diazinon + Araclor 5460 (1 : 4), applied to pine foliage: Gave 92% kills of Musca domestica after 30 days; 77% after 60 days; Diazinon (alone) and Diazinon + Araclor 1 : 1 were ineffective after 4 days.

10) Effect of Diazinon and other compounds on beneficial insects, placed on plants previously dusted with insecticide (5% dusts) applied by the vacuum method. Adult insects; laboratory cage tests: 1404

Insecticide Dust		% Mortality 24 Hrs Of		
		Collops vittatus	Hippodamia convergens	Coleomegilla maculata
Diazinon	(4%)	37	66	100
Chlorthion		64	82	100
Malathion		47	90	100
Parathion	(2%)	65	78	98
DDT		38	6	32
Perthane		23	6	12
Strobane		10	18	12
Heptachlor	(2.5%)	41	30	38
Toxaphene	(10%)	32	12	36
Endrin	(1%)	27	10	18
Dieldrin	(2%)	36	4	24
Control		11	4	0
Lowest Sig. Diff. 5% level		20	24	26

11) Diazinon and other insecticides, comparative acaricidal effectiveness: (Also consult the general treatment, in this work, titled Miticides or Acaricides) vs. developmental stages of Tetranychus bimaculatus, placed on bean leaves previously treated in a settling tower by the method of Ebeling and Pence; E = Emulsifiable Concentrate, W = Wettable Powder Formulation: 905

Acaricide	LC$_{50}$ (g/100cc) 48 Hrs.			
	Adult	Larva	Egg	Adult On Leaf Surface Opposite Treated Surface
Diazinon W	0.012	0.028	0.18	0.115
Demeton (Systox®) E	.0022	.0028	.097	.003
EPN W	.0048	.0077	.46	.076
EPN E	.0025	.0047	.23	.042
Malathion W	.0042	.0115	.84	.125
Malathion E	.0025	.0073	.32	.084
Parathion W	.0045	.010	.37	.027
Parathion E	.0056	.013	.19	.021

b) LD_{50}, LD_{100} of various acaricides, in acetone solution, by topical application to adult ♀ Tetranychus bimaculatus: 1121

Acaricide	LD_{50}		LD_{100}		
	(?) μg/mite	mg/k	(?) μg/mite	mg/k	
Diazinon	4.4	240	.2	100	(sic)
Parathion	1.8	90	4	200	
Systox	.4	20	.76	38	
Pyrazoxon	.76	3.8	.1	5	(sic)
Pyrazothion	2.2	120	1.2	60	(sic)
DMC	4.2	210	8	400	
Chlorobenzilate	2	100	3	150	
Etoxinol	3	150	7.8	390	

c) Diazinon and other compounds vs. Metatetranychus ulmi on Northern Spy Apple Trees: 1990

Acaricide	Dosage/100 Gals.	% Reduction (Days After Spraying)		
		3 days	10 days	17 days
Systox® (42% liquid)	2 oz	98.5	100	100
"	4 oz	99.1	100	99.9
Ethoxymethyl di(p-chlorophenyl) carbinol (25% emuls)	1 pint	98.5	87.5	83.7
Chlorobenzilate (25% emuls.)	1 pint	99.0	95.8	95.6
Diazinon (25% emuls.)	1 teaspoon	95.6	94.6	89.5
O,O-Diethyl-O-5(3-methylpyrazolyl) thiophosphate(25% emuls.)	1 pint	96.2	99.8	99.8
Diethyl 5-(3-methylpyrazolyl) phosphate (25% emuls.)	1 pint	95.3	98.8	98.6
Malathion (25% wett. pwdr.)	2 lb	97.2	99.6	98.6
Malathion (50% emuls.)	1 pint	96.5	98.7	96.9
Parathion (15% wett. pwdr.)	1 lb	98.7	99.8	99.5
NPD (25% wett. pwdr.)	2 lb	99.3	98.5	97.3
Aramite (15% wett. pwdr.)	1.5 lb	98.1	98.5	97.1
Control (Average number hatched mites/leaf.)		239	104	59

12) Diazinon and other insecticides: Comparative effectiveness vs. certain lice of livestock: 2862

Insecticide	Concentration (%)	Vs. Haematopinus eurysternus	
		% kill 24, 48 Hrs.	Weeks Effective
Diazinon	.25	100	2
"	.1	100	2
"	.05	100	1
"	.01	95	1
"	.005	25	1
"	.002	5	1
Pirazinon	.25	100	3
EPN	.05	100	1
"	.01	100	1
"	.005	100	1
"	.002	25	0
Tetraethyl dithiopyrophosphate	.05	100	1
Bayer 21/199	.25	100	2
" "	.2	100	2
" "	.1	100	1
" "	.05	100	1
Dipterex	.25	100	1
"	.1	100	0
Chlorthion	.25	100	1
Parathion	.05	100	3
"	.01	100	3
"	.005	25	0
Malathion	.5	100	2
"	.05	100	1
DDT	.5	100	4
"	.25	100	3
Toxaphene	.5	100	4
Strobane	.5	100	4
2-Pivalyl indanedione	1.0	100	3
" "	.5	100	2
" "	.25	100	2
" "	.1	100	2
" "	.05	100	2

Insecticide	Concentration (%)	Vs. Bovicola caprae and B. limbatus	
		% kill 24, 48 Hrs.	Infestation After 4 wks.
Diazinon	.05	100	0
"	.025	100	0
"	.05	100	0
"	.005	100	light
EPN	.002	100	0
Bayer 21/200	.002	25	light
Bayer 21/199	.002	100	0
Dipterex	.1	100	light
"	.05	100	light
"	.025	100	light
"	.01	100	light
"	.002	100	light
Chlorthion	.002	100	0
Malathion	.25	100	0
"	.1	100	0
"	.05	100	0
"	.025	100	0
Isodrin	.05	100	0
Endrin	.05	100	0
Strobane	.2	100	0
"	.1	100	0
DDT	.25	100	0

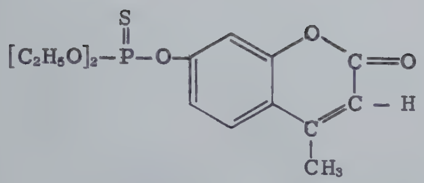
13) Diazinon and synergism with piperonyl butoxide: 2576

- a) In topical application to Musca domestica, piperonly butoxide markedly enhances the lethal effect of diazinon (as well as Dipterex®[Bayer L 13/59]). This is in contrast to the antagonistic effect exerted by piperonyl butoxide on Malathion.
- b) PBO exerts no effect in vitro on the anti-choline esterase activity of Diazinon for bovine erythrocyte and Musca choline esterases from DDT-R and DDT-non R biotypes.

62

O,O-DIETHYL O-(4-METHYL-7-COUMARINYL) THIONOPHOSPHATE

(Potasan®; E 838; Diethylmethylcoumarinyl thiophosphate; O,O-Diethyl-O-(4-methylumbelliferone)ester of thiophosphoric acid; O,O-Diethyl-O-(2-keto-4-methyl-7-α′, β′-benzo-α′ pyranyl) thiophosphate; O,O-Diethyl thiophosphoric ester of 7-hydroxy-4-methylcoumarin)



Molecular weight: 329.317

GENERAL

[Refs.: 2773, 2120, 1807, 1801]

An orthothiophosphate insecticide, related to parathion, q.v., and prepared in a similar manner by condensation of β-methyl umbelliferone with diethyl thiophosphoryl chloride. A selective toxicant for insects, exerting both a contact and stomach, but only a slight fumigant, action. Reported to be of high toxicity for Colorado potato beetle adults and larvae, but of low toxicity for aphids. The promise shown in laboratory tests against Metatetranychus ulmi (= Paratetranychus pilosus) has, reportedly, not been maintained in the field, where 2 applications, at 0.01%, failed to control. Also consult the general treatment, in this work, of Organic Phosphates.

PHYSICAL, CHEMICAL

Colorless, crystalline solid of slight, aromatic odor; m.p. 38°C; $d_{4^\circ}^{38^\circ}$ 1.26; $n_D^{37^\circ}$ 1.5685; virtually insoluble in water; readily soluble in most organic solvents; moderately soluble in light petroleum oils; stable in water or in aqueous emulsion in which it displays, at p H 7-8, a blue fluorescence. 2773, 2231

- a) Formulated as "Potasan G liquid" combined with BHC γ -isomer (lindane), it is recommended specifically for Leptinotarsa decemlineata, when used at a strength not less than 0.05% at 600 liters/hectare.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)		
Mouse	or	LD_{50}	98.5 ± 5.0		1057
Rat ♂	or	LD_{50}	42.0 ± 3.1	Parathion = 6-15 mg/k (LD_{50}).	1057
Rat ♀	or	LD_{50}	19.0 ± 2.5		1057
Rat	ip	LD_{50}	15.0		861
Guinea Pig	or	LD_{50}	25.0 ± 2.3		1057
Rabbit	ct	LD_{50}	ca 300	Parathion = 40-50 mg/k (LD_{50}).	1952

2) Pharmacological, pharmacodynamical, physiological etc.,

- a) Consult general treatment of organic phosphate insecticides.

3) Phytotoxicity:

- a) No data available to this compilation at the time of preparation.

4) Toxicity for insects and acarines:

- a) No quantitative data available to this compilation.

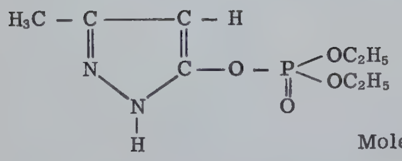
b) The high degree of toxicity reported for Leptinotarsa decemlineata and the low toxicity for aphids has been mentioned above. Also mentioned has been the reported failure of Potasan® to fulfill, in the field, the promise shown in the laboratory as a toxicant for Metatetranychus ulmi. 2120, 1807

c) Screening test data indicated, under the conditions and standards adopted for such tests, that: 1801
   (1) Potasan® achieved the highest category of effectiveness when tested against body lice (Pediculus humanus corporis) as insecticide, and a high rating as a louse "knockdown" toxicant. A high rating was recorded for Potasan® as a mosquito larvicide and residual toxicant for Musca domestica. The rating as a space spray for Musca was moderate.

63

O,O-DIETHYL O-(3-METHYLPYRAZOLYL) - (5) PHOSPHATE

(Pyrazoxon; Methylpyrazolyl diethylphosphate; 3-Methylpyrazolyl-(5)-diethylphosphate; G-24483 [Geigy].)



Molecular weight: 235.199

GENERAL

[Refs.: 1317, 1121, 2120, 2213, 2651, 1285, 2942]

An insecticide of the general class commonly known as organic phosphates or "organophosphorus" insecticides, recently (1952) brought forward experimentally. Pyrazoxon is a potent insecticide related to Pyrolan, q.v., both being derived from pyrazolone. The dimethyl carbamate portion of the Pyrolan molecule is replaced, in the case of Pyrazoxon, by the diethyl ester of orthophosphoric acid. In contrast with Pyrolan, Pyrazoxon is highly active against mites and lice. Pyrazoxon possesses systemic insecticidal, acaricidal, action via the fluids and sapstream of Pyrazoxon treated plants. Also consult Pyrazothion, the diethyl thiophosphoric acid ester analog of Pyrazoxon. Pyrazoxon is endowed with powerful contact, fumigant, and systemic activity. Also see, in this work, general treatments of Organic Phosphates and Systemic Insecticides.

PHYSICAL, CHEMICAL

A yellowish liquid (technical) which decomposes under distillation; $d_{4^\circ}^{20^\circ}$ 1.001; soluble to less than 1 part in 100 parts of water; not soluble in petroleum oils; soluble in alcohol, acetone and xylene. 1317

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) Mouse oral LD_{50} = 4 mg/K, an exceedingly high mammalian toxicity. 1121

2) Pharmacological, pharmacodynamic, physiological, etc., higher animals:
   a) No specific data available to this compilation, but presumably, as in case of other members of this general class of insecticides, Pyrazoxon, or its metabolites, inhibit choline esterase(s), with consequent cholinergic intoxication through disturbance of systems in which acetylcholine plays a part.

3) Phytotoxicity:
   a) No data available, but its use as a systemic insecticide suggests that the phytotoxic hazard, at effective concentrations, is not too great to preclude its use on plants.

4) Toxicity for insects and acarines:
   a) Comparative activity of Pyrazoxon and other insecticides vs. certain aphids: 1285
      (1) As sprays. Contact action:

Insecticide	Insect	Concentration (%)	% Mortality At Hrs After Treatment			
			24 hrs	72 hrs	120 hrs	456 hrs
Pyrazoxon	Aphis pomi	0.02	96.5	100	98.5	96
Pyrazothion	"	.02	98.2	99.7	99.4	100
Diazinon	"	.02	85.7	90.9	73	30
OMPA (Schradan)	"	.06	73.9	91	97.7	100
Pyrazoxon	Sapphaphis plantaginea	.02	99.3	100	100	100

(1) As sprays. Contact action:

Insecticide	Insect	Concentration (%)	% Mortality At Hrs After Treatment 24 hrs	72 hrs	120 hrs	456 hrs
Pyrazothion	Sapphaphis plantaginea	.02	5	100	100	100
Diazinon	"	.02	94.8	100	100	100
OMPA	"	.06	—	—	—	—

			72	120	240	288	360	504 Hours
Pyrazoxon	Phylloxera vastatrix	.04	82	90	76	82	86	61
Pyrazothion	"	.02	24	—	78	—	—	54
Diazinon	"	.04	83	94	90	100	94	96
Systox	"	.04	78	95	57	90	58	92
Isolan	"	.008	25	—	47	—	—	49
Control	"	—	—	38	13	11	2	4

(2) Systemic action vs. Tetranychus bimaculatus on bean plants, root-dipped in the toxicants in Knop's solution:

Toxicant	Concentration g/100 l	Mite Numbers At								
		Start			4 Days Later			6 Days Later		
	(stage)	mobile	resting	eggs	mobile	resting	egg	mobile	resting	egg
Pyrazoxon	10	12	5	49	0	0	14	0	0	2
"	20	14	8	22	0	0	8	0	0	1
Pyrazothion	10	21	6	24	14	1	36	16	0	40
"	20	19	11	14	15	0	15	8	0	26
Diazinon	10	18	12	19	9	4	23	13	0	30
"	20	17	24	9	4	8	28	9	0	29
Systox	10	20	0	12	0	0	12	0	0	6
"	20	14	4	34	0	0	34	0	0	26
OMPA	10	11	8	45	0	0	38	2	0	31
"	20	14	4	31	0	0	31	0	0	27
Control	—	27	13	18	48	26	121	156	29	203

(3) LD_{50}, LD_{100}; topical application in acetone solution to T. bimaculatus ♀: 1121

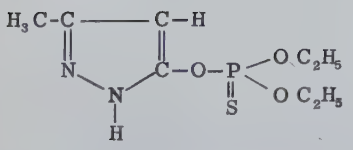
Toxicant	LD_{50} (??) μg/mite	mg/K	LD_{100} (??) μg/mite	mg/k	
Pyrazoxon	0.76	3.8	0.1	5.0	(sic)
Pyrazothion	2.2	120	1.2	60	(sic)
Diazinon	4.4	240	0.2	100	(sic)
Parathion	1.8	90	4.0	200	
Systox	0.4	20	0.76	38	
Etoxinol	3.0	150	7.8	390	
Chlorobenzilate	2.0	100	3.0	150	
DMC	4.2	210	8.0	400	

(4) Pyrazoxon and other acaricides in field trials vs. Metatetranychus ulmi on Northern Spy apple orchards; New York State, 1952: 1990

Toxicant	Dosage/100 gal	% Reduction At Days After July 4 Spraying 3 days	10 days	17 days
Pyrazoxon (25% Emuls.)	1 pint	95.3	98.8	98.6
Pyrazothion (25% Emuls.)	1 pint	96.2	99.8	99.8
Systox (42% Liquid)	2 ounces	98.5	100	100
Systox (42% Liquid)	4 ounces	99.1	100	99.9
Ethoxymethyl di(p-chlorophenyl) carbinol (25% Emuls.)	1 pint	98.5	87.5	83.7
Chlorobenzilate (25% Emuls.)	1 pint	99.0	95.8	95.6
O,O-diethyl-O-(2-isopropyl-4-methylpyrimidyl)-(6)-thiophosphate (25% Emuls.)	1 tp	95.6	94.6	89.5
Malathion (25% Wett. Pwdr.)	2 lbs	97.2	99.6	98.6
Malathion (50% Emuls.)	1 pint	96.5	98.7	96.9
Parathion (15% Wett. Pwdr.)	1 lb	98.7	99.8	99.5
NPD (25% Wett. Pwdr.)	2 lb	99.3	98.5	97.3
Phenyl mercuric acetate (10% liquid)	0.5 pint	91.7	71.5	—
2-Heptadecyl glyoxalidine acetate (34% Liquid)	2 pints	96.6	67.9	—
Sulphenone® (50% Wett. Pwdr.)	3 lbs	99.4	94.9	94.6
Aramite® (15% Wett. Pwdr.)	1.5 lbs	98.1	98.5	97.1
Control (Average Number Hatched Mites/Leaf)	—	239	104	59

64

O,O-DIETHYL O-(3-METHYLPYRAZOLYL) - (5) THIOPHOSPHATE (Pyrazothion; Methylpyrazolyl diethylthiophosphate; G-23027 [Geigy].)



Molecular weight 236.249

GENERAL

[Refs.: 1317, 1121, 2120, 2651, 1285, 1990]

A new insecticide, brought forward experimentally in 1952, of the general class commonly referred to as organic phosphates or "organophosphorus" insecticides. Pyrazothion possesses a high toxicity for a wide range of insects, and has shown excellent promise as a contact acaricide. Pyrazothion is closely related to Pyrazoxon, q.v., and like it is related to Pyrolan, q.v. In the case of Pyrazothion, the diethylcarbamate portion of the Pyrolan molecule is replaced by the diethyl ester of thiophosphoric acid. Pyrolan, Pyrazothion and Pyrazoxon share in common a pyrazolone nucleus. Pyrazothion has shown itself (in some tests) to be superior to parathion in acaricidal effectiveness. Its order of acaricidal effectiveness lies between that of Diazinon and Pyrazoxon, as tested vs. Tetranychus bimaculatus. Field tests have shown high efficacity vs. Metatetranychus ulmi. In terms of systemic activity vs. T. bimaculatus, Pyrazothion has shown itself poor in systemic action via bean plants, root-dipped in pyrazothion solutions, as compared to Pyrazoxon under similar trial conditions. This last may reflect the much lesser water solubility of Pyrazothion vis-a-vis Pyrazoxon.

PHYSICAL, CHEMICAL

A yellow-brown liquid (technical) which decomposes on distillation; slightly soluble in water (to 0.01%); virtually insoluble in petroleum oils; miscible with alcohol, acetone and xylene. 2120 1317

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	12	As a 20% emulsion.	1121
Rat	or	LD_{50}	36	As a 20% emulsion.	1121

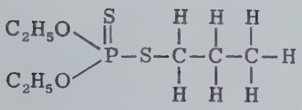
a) Less toxic for the mouse than Pyrazoxon.
b) Shows no cumulative tendency in the mammalian body.
c) Mode of action presumably, as for others of its general class, by cholinergic intoxication.

2) Phytotoxicity:
a) No data have indicated phytotoxic activity at dosages insecticidally and acaricidally effective.

3) Toxicity for insects, acarines:
a) Consult, in this work, Pyrazoxon, where, on a comparative toxicity basis, may be found all the data available to this compilation on the toxicity of Pyrazothion for insects and phytophagous mites.

65

O,O-DIETHYL S-PROPYL MERCAPTOMETHYL DITHIOPHOSPHATE (TM 12009)



GENERAL

An experimental systemic insecticide which has been tested on cotton insects placed on cotton plants grown from seed treated at the rate of 4 lbs TM 12009 per 100 lbs cotton seed, with the results shown below. Also consult TM 12008, TM 12013. 1660

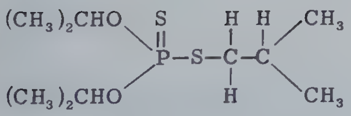
Insect	% Mortality At Stated Periods After Seed Treatment					
	Seedlings	Plants in Cans			Field Plants (Cage Tests)	
	1 wk	2 wks	3 wks	4 wks	5 wks	6 wks
Anthonomus grandis (Adult)	100	83	31	0	0	0
Anthonomus (Toxaphene control [2 lbs/acre])	84	62	59	60	53	42
Alabama argillacea (New Hatched Larva)	100	100	93	26	0	0

a) At three weeks after seed treatment 100% mortalities were registered for *Aphis gossypii*, *Tetranychus desertorum*, *Psallus seriatus* (adult), *Bucculatrix thurberiella* (newly hatched larva), *Estigmene acraea* (newly hatched larva) on plants grown from treated seed.

b) At three weeks some effect was shown against *Frankliniella tritici*, but none against *Heliothis armigera* larvae.

66

O,O-DIISOPROPYL S-ISOPROPYL MERCAPTOMETHYL DITHIOPHOSPHATE (TM 12013)



1660

GENERAL

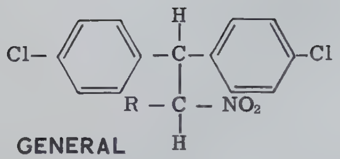
An experimental systemic insecticide which has been tested on cotton insects placed on cotton plants grown from seed treated at the rate of 4 lbs TM 12013 per 100 lbs cotton seed, with the results shown below. Also consult TM 12008, Tm 12009.

Insect	% Mortality At Stated Periods After Seed Treatment					
	Seedlings	Plants In Cans			Field Plants (Cage Tests)	
	1 wk	2 wks	3 wks	4 wks	5 wks	6 wks
Anthonomus grandis (Adult)	83	12	0	0	0	0
Anthonomus grandis Toxaphene control (2 lbs/acre)	84	62	59	60	53	42
Alabama argillacea (New Hatched Larva)	100	88	4	0	0	0

a) At three weeks after seed treatment 100% mortalities were registered for *Aphis gossypii*, *Tetranychus desertorum*, *Psallus seriatus* (adult) on plants grown from treated seed. Slight effect was noted vs. *Bucculatrix thurberiella* (newly hatched larva), and *Estigmene acraea* (newly hatched larva). No effect was manifested vs. *Heliothis armigera*.

67

DILAN® (A mixture, as specified below.)



Where R = CH_3-(Prolan®); CH_3CH_2-(Bulan®)

GENERAL

Dilan® is a mixture of two nitroalkyl DDT analogues, 2-nitro-1, 1-bis-(p-chlorophenyl) butane [1,1-bis-(p-chlorophenyl)-2-nitrobutane] and 2-nitro-1, 1-bis(p-chlorophenyl) propane [1,1-bis-(c-chlorophenyl)-2-nitropropane] named respectively in trade as Bulan® and Prolan®. The mixture comprises 52.2% by weight Bulan®, 26.2% by weight Prolan® and 19.6% by weight of related substances. Thus, Dilan® contains the two most effective of the nitroalkyl analogues of DDT. Prolan® and Bulan® have been reported to be more effective insecticides than DDT for Epilachna varivestis, various aphids, and thrips. Alternative names or designations for the components of Dilan® are: Bulan®: DNB, CS 674 A; Prolan®: DNP, CS 645 A. 575

PHYSICAL, CHEMICAL

At room temperatures, a brown, sticky, semi-solid plastic of almond-like odor; like DDT, Dilan® is a mixture of the isomers of its components Bulan® and Prolan® chiefly the active p,p′-isomers with the o,p′-isomers forming much of the approximately 20% of related compounds present in the Prolan® and Bulan® mixture which makes up Dilan®; Dilan® is liquid at > 65°F (ca 18°C) the m.p. of Prolan® = 80.5-81.5°C, Bulan® = 66.5°-67.5° C; $d^{15°}_{15°}$ 1.28; vapor pressure (volatility) very low; virtually insoluble in water; limited solubility in petroleum oils and ethanol; high solubility in methanol and aromatic solvents such as xylene; unstable in the presence of alkalis; susceptible to oxidation with formation of substances non-toxic for insects.

a) Formulations: Liquid concentrate (Dilan® 80%, xylene 20%); emulsifiable concentrates e.g. Dilan® 25 EM, of 25% Dilan® content; wettable powders e.g. Dilan® 50 DC, 50% Dilan® on a Celite® 800 base; 1-2% dusts. Ordinary dilutions for use contain 1/2 lb Dilan® per 100 gallons.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) The toxic hazard is reported to be ca. 1/2 that presented by DDT; classified, from the standpoint of industrial hygiene, as slightly toxic in single dose. 574, 779

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	ca 1100	Compare with 135 mg/k for DDT, 3000 mg/k for methoxychlor.	89
Mouse	ip	LD_0	400	5 Animals per test.	779
Mouse	ip	LD_{50}	600	5 Animals per test.	779
Mouse	ip	LD_{100}	800	Compare with 135 mg/k for DDT, 3000 mg/k for methoxychlor.	779
Rat	or	LD_{50}	4000	= LD_{50}, oral, for Prolan®.	1951
Rat	or	LD_{50}	330	= LD_{50}, oral, for Bulan®.	1951
Rat	ct	LD_{50}	♀5900; ♂6900	LD_{50} for Prolan®, Bulan® = > 4000 mg/k.	89

2) Chronic toxicity for higher animals:

a) Dogs: Receiving 125 ppm in diet for 20 weeks (immature animals) showed no adverse effects; haematological findings: Normal. At autopsy of some subjects, moderate liver damage was noted; no splenic damage. Animals which received 62.5 ppm in the diet showed but slight hepatic damage. No morphological evidence of interference with liver function was noted. Histological examination of livers of surviving animals showed the hepatic damage to be completely reversible. 779

b) Rabbits: Receiving skin application of undiluted Dilan® 25 EM (25% emulsifiable concentrate) manifested, in 24 hrs exposures, severe irritation. At 1:800 dilution (the concentration recommended for use) Dilan® 25 EM proved non-irritant to intact, but slightly irritant to abraded skin. Dilution at 1:2000 of Dilan® 25 EM proved non-irritating, either to intact or abraded skin. Emulsion formulations without Dilan®, similarly tested, were found to be equally irritating. 779

c) Warning is provided on the Dilan® labels of the irritant property for eyes and skin and the skin-penetration properties. Warning against inhalation, skin contact, food contamination is likewise provided. 779

d) Other comments:

(1) Calves, sprayed with 4% Dilan® wettable powder suspension, chickens, dipped in like suspension, gave no sign of injury. 89

(2) Neither the acute or chronic dosage for man is known.

(3) Rats, fed a diet with 625 ppm Dilan® for 1 year, showed no adverse growth effects, (DDT at 400 ppm for ♀♀ and 800 ppm for ♂♂ for 12 weeks reported to retard growth).

3) Pharmacological, pharmacodynamical, physiological etc.

a) The specific properties of Dilan®, or its components Prolan® and Bulan® are unknown. By analogy of structure with DDT and methoxychlor, the mode of action, etc., might be expected to be similar. Consult DDT and others. 89

b) Symptoms in animals resemble those attending intoxication by other chlorinated hydrocarbons. Stored in the fat and excreted in the milk of mammals. 267 89

4) Phytotoxicity:

a) For cantaloupes 1:800 (recommended) dilutions of emulsifiable concentrate containing 25% Dilan® were non-injurious; 1:400 dilutions induced injury in very young plants. Lima bean (young plants) sprayed 5 times with dilutions of 0.5, 0.25, 0.12, 0.08% appeared unharmed. No reports of damage to peach trees, tomato, or rose plants. 779

5) Toxicity for insects; insecticidal activity:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Musca domestica (adult)	Contact Spray	LC_{50} 24 hr	0.72 mg/cc	KD 10 min at LC_{50}ca 30%; Peet-Grady Method.	2033
Musca domestica (adult) (laboratory strain)	Topical	LD_{50} 24 hr	2.4 μg/fly	At 80°F; a Dilan non-R strain.	371
Musca domestica (adult)	Topical	LD_{50} 24 hr	> 100 μg/fly	At 80°F; strain exposed for 5 generations.	371
Anthonomus grandis (adult)	or + Contact	LD_{50}	11.4 lb/acre	Dusts of Prolan®.	2276
Anthonomus grandis (adult)	or + Contact	LD_{50}	16.7 lb/acre	Dusts of Bulan®.	2276

b) Comparative toxicity for insects, Dilan® and other insecticides:

(1) As insecticidal emulsions in control of Musca domestica larvae in breeding media: 1326

Insecticide	% Mortality At (mg Active Ingredient/k Medium)					
	50 mg	20 mg	15 mg	10 mg	5 mg	2 mg
Dilan®	99.5	100	—	100	5	—
DDT	100	—	—	—	—	—
Methoxychlor	25	—	—	—	—	—
Toxaphene	100	100	—	100	75	0
Lindane	—	99.5	—	60	—	—
Chlordane	—	—	100	—	—	75
Aldrin	—	—	100	100	100	97.5
Dieldrin	—	100	—	100	100	94
Heptachlor	—	100	—	—	100	90

(2) Toxicity of Dilan® and other compounds for Musca domestica (adult); tested by Peet-Grady Method; contact sprays: 2033

Insecticide	Concentration (mg/cc) For 50% Kill In 24 Hrs.	KD 10 Minutes (%)
Dilan®	0.72	ca. 30
Dieldrin	.017	0
Parathion	.02	0
Methyl parathion	.025	0
Lindane	.046	0
Heptachlor	.052	0
Aldrin	.056	0
TEPP	.069	ca. 70
Chlordane	.25	0
DDT	.35	0
Malathion	.48	0
Toxaphene	.68	0
Tetrapropyl dithiophosphate	.69	0
Isolan	1.15	100
Allethrin	1.5	100
Pyrolan	5.5	100

(3) Toxicity of Prolan®, Bulan® and other compounds as dusts, in combined oral and contact action (insects placed on dusted food plant) for Anthonomus grandis (adult; Boll weevil): 2276

Insecticide	LD_{50} (Lbs Active Ingredient/Acre)
Prolan®	11.4
Bulan®	16.7
Dieldrin	.9
Aldrin	1.1
BHC (tech)	1.0
Chlordane	10.1
Toxaphene	6.4
DDT	9.1

(4) Prolan®, Bulan® and Prolan® + Bulan® combinations; toxicity for 4 species of cotton insects. Applied as dust concentrates with 50% active ingredient: 2748

Insecticide	Average Mortality (%) After 5 Days Of			
	Anthonomus grandis (adult)	*Heliothis armigera* (3rd instar)	*Alabama argillacea* (3rd instar)	*Estigmene acraea* (3rd, 4th instar)
Prolan 2.5%, Bulan 5%	31	3	—	91
Prolan 5%, Bulan 10%	69	91	—	100
Prolan 10%, Bulan 20%	80	94	—	100
Prolan 2.5%	32	35	—	—
Prolan 5%	48	29	56	—
Prolan 10%	59	32	80	—
Prolan 20%	—	—	92	37
Bulan 5%	53	55	97	96
Bulan 10%	70	85	100	100
Bulan 20%	78	92	100	100
Toxaphene 20%	99	88	98	50

(5) Prolan® and Bulan® in control of *Heliothis armigera* on corn. Effectiveness measured as % of clean ears of corn in spray and dust treatments. Application directly to silk channel of corn ears at a dosage of ca. 1-2 lbs per acre: 1877

Insecticide	% Clean Ears; Two Plantings		Comparative, % Clean Ears With Sprays, Dusts	
	1	2		
Prolan (spray, emulsion conc.)	82.0	85.7	Prolan	77.4
Bulan (spray, emulsion conc.)	78.3	75.9	Bulan	74.9
Prolan (dust, 5% in fuller's earth)	76.0	65.9	DDT	83.8
Bulan (dust, 5% in fuller's earth)	65.2	79.4	DDD	83.8
Control	52.9		Toxaphene	75.5
			Control	52.9

Lowest Significant Difference 1% level=15.7

(6) Dilan® and other compounds; comparative toxicity for *Cirphis unipuncta* (larva): 3268

Toxicant	Topical Application		Oral (On Leaves)		Ratio LD_{50} To LD_{99}	
	LD_{50} ($\mu g/g$)	Ratio to Parathion	LD_{50} $\mu g/g$	Ratio to Parathion	Topical	Oral
Dilan®	8.8	2.4	11.5	4.6	5.4	5.0
Dieldrin	8.3	2.2	4.6	1.8	3.1	3.8
Parathion*	3.7	1.0	2.5	1.0	3.4	8.5
DDT	193.0	52.2	45.7	18.3	4.7	22.8
Chlordane	117.5	31.6	78.2	31.3	4.9	4.7
Toxaphene	56.2	15.2	34.1	13.6	4.7	2.9
Lindane	28.1	7.6	27.9	11.2	3.2	5.1
Aldrin	19.8	5.4	11.4	4.6	3.7	24.7

* Parathion yielded the fastest kill, followed, in order, by Dilan®, Lindane, DDT.

7) Field experiences; insecticidal activity of Dilan®:

a) Sprayed at a concentration of 0.006% in water and as dusts, 0.12% Dilan® gave 100% kills of *Epilachna varivestis* larvae. 779

b) Sprayed at concentrations of 0.012% and at 0.62% in dust yielded 100% kills of *Macrosiphum pisi*. 779

c) Screening tests revealed effectiveness for *Curculio*, Oriental fruit moth and "cat facing" insects on peaches; very effective for tomato fruit worm and tobacco horn worm. 779

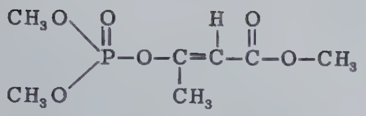
d) Vs. *Estigmene acraea*: Very superior to toxaphene (which, as a 20% dust, gave 90% kill) in control of. 2748

e) Vs. *Heliothis armigera*: Inferior to DDT in control of. 1877

68

DIMETHYL-1-CARBOMETHOXY-1-PROPEN-2-YL PHOSPHATE

(Compound 2046, Shell Chem. Corp; Dimethyl carbomethoxypropenyl phosphate; Dimethyl methoxycarbonylpropenyl phosphate.)



$(\mathrm{CH_3O})_2\overset{\mathrm{O}}{\overset{\|}{\mathrm{P}}}-\mathrm{O}-\underset{\mathrm{CH_3}}{\mathrm{C}}=\overset{\mathrm{H}}{\mathrm{C}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{O}-\mathrm{CH_3}$

Molecular weight: 221.049

GENERAL

[Refs.: 599, 600, 2651, 2942]

An organophosphorus compound of recent introduction, which has shown promising systemic acaricidal properties. Indications are that it acts in the plant as an endolytic systemic toxicant, in the sense proposed by Ripper.

PHYSICAL, CHEMICAL

A light, yellow-green liquid; b.p. 106-107°C at 1 mm Hg; $d^{20°}_{4°}$ 1.25; $n^{20°}_{D}$ 1.4494; volatility slight (loss from sprayed glass plates is at the rate of 3% per hour at ordinary temperatures;) miscible with water; moderately stable in neutral solution, activity being retained for at least 7 days.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	
Mouse ♂	or	LD_{50}	7.8 (6.8-8.9)	1837
Mouse ♀	or	LD_{50}	4.3 (2.7-6.9)	1837
Rat ♂	or	LD_{50}	6.8 (5.4-8.6)	1837
Rat ♀	or	LD_{50}	6.0 (5.2-7.0)	1837
Rat ♀	ip	LD_{50}	1.5 (1.3-1.7)	1837
Rabbit	ct	LD_{50}	33.8 (12.6-55.0)	1837

a) The foregoing data indicate a high toxicity, by all routes, for warm blooded animals.

b) An active inhibitor *in vitro* of mammalian acetylcholine esterase. ID_{50} for human erythrocyte Ch E = 2.3×10^{-6} M.

2) Pharmacological, pharmacodynamical, physiological, etc.:

a) Consult the general treatment, in this work, of Organic Phosphate Insecticides.

3) Phytotoxicity:

a) Since the substance has been tested and found to be an effective systemic acaricide at least on some plants, it may be presumed to be non-phytotoxic for some plants if not all.

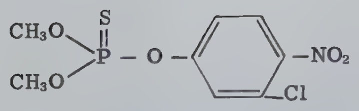
4) Toxicity for insects; insecticidal activity:

a) Data are very meager. A rapid movement into the exposed plant is indicated for dimethyl carbomethoxypropenyl phosphate, the entry into the plant taking place to the fullest extent within a few minutes of application. Translocation from the roots to the upper leaves of *Vicia faba* plants is rapid. There is evidence of outward movement into the environment with the transpiration stream. Toxicity of the treated plant for insects and acarines is markedly reduced in 24 hours. 599

69

O,O-DIMETHYL O-3-CHLORO-4-NITROPHENYL THIONOPHOSPHATE

(Chlorthion®; Bayer 22/190; O,O-Dimethyl-O-3-chloro-4-nitrophenyl thiophosphate; Dimethyl 3-chloro-4-nitrophenyl thiophosphate; p-Nitro-m-chlorophenyl dimethylthionophosphate; O,O-Dimethyl O-3-chloro-4-nitrophenyl phosphorothioate.)



Molecular weight: 297.598

GENERAL

[Refs.: 2768, 2231, 2120, 3204]

An organophosphorus insecticide and acaricide, of recent (1952) introduction. Closely related to parathion methyl parathion and Experimental Insecticide 4124. Chlorthion® is a relatively non-toxic insecticide for mammals yet being of high insecticidal activity. Chlorthion® has been extensively tested in Europe, the United States and elsewhere and has been found to control practically all insects for which parathion is effective being, in addition, useful against Anthonomus grandis and related Coleoptera. Chlorthion® holds considerable interest as a toxicant for DDT-Resistant Musca domestica. It combines a relatively low hazard and high margin of safety for higher animals with effectiveness, at relatively low dosages, for insects. Consult the section in this work given over to a general treatment of Organic Phosphates.

PHYSICAL, CHEMICAL

A yellowish-brown, viscous liquid of characteristic ester-like odor; b.p. 112°C at 0.04 mm Hg, 121°C at 0.08 mm Hg, 136°C at 0.2 mm Hg; $d_4^{20°}$ 1.437; $n_D^{20°}$ 1.5661; v.p. at 10°C 7×10^{-6} mm Hg, at 20°C 22×10^{-6} mm Hg; at 30°C 70×10^{-6} mm Hg; volatility: at 20°C 0.07 mg/m³, at 30°C 0.3 mg/m³, at 40° 0.95 mg/m³; slightly soluble in water (ca 1 part : 25,000 parts); readily soluble in most organic solvents for example benzene, toluene, alcohols, ethers, fatty oils, olive oil and peanut oil; slightly soluble in petroleum ether; hydrolizes quickly in alkaline media; not stable in aqueous dilutions at p H > 7.5; tends, like methyl parathion, to hydrolize under certain conditions; incompatible with Bordeaux mixture, lime-sulfur, lime; compatible with DDT, lindane, fixed coppers, wettable sulfur; believed to be compatible with most other fungicides, insecticides.

a) Formulation: 25% wettable powder; spray concentrate with 4 lbs. active ingredient per gallon; 3% dusts; Chlorthion® Technical (available for special purposes only).

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	
Rat	or	LD_{50}	1500	854
Rat	or	LD_{100}	500	2768
Rat	ip	LD_{50}	750	854

(1) About 0.2 as toxic orally for the rat as the diethyl ester; slight changes in substituents and position modify toxicity e.g. dimethyl 2-chloro-4-nitrophenyl thiophosphate, q.v., has an LD_{100} (oral) for rats of 200 mg/k. 2768

2) Chronic and sub-chronic toxicity for higher animals:

a) 50 mg/k daily for 60 days, in the diet of rats was tolerated; no mortality; 100 mg/k daily over a 60 day period gave 40% mortality among exposed animals. 854, 3204

b) 1 cc (ca 1400 mg/k), applied to shaved abdominal skin of rabbits as undiluted Chlorthion® yielded no symptoms of intoxication. 3204, 1474

3) Pharmacological, pharmacodynamical, physiological, etc.

a) Chlorthion® is an active in vitro inhibitor of rat brain cholinesterase at a concentration of 5×10^{-6} M. Low mammalian toxicity in vivo is ascribed to slow absorption by tissues. Atropine sulfate is stated to be antidotal. 2120, 3204

b) The mode of toxic action may be attributed to the cholinesterase inhibition as a primary factor, with the signs and symptoms of cholinergic intoxication following upon it. (Consult the general treatment of Organic Phosphates in this work.) 2231, 3204, 713

c) Given at 200 mg/k/day to rats, Chlorthion® brought about swift decline of cholinesterase to ca. 1/4th the normal level; the dosage was not tolerable for more than 5-10 days. Daily doses at 50 and 100 mg/k caused a decline of cholinesterase activity to 50% of normal; the 50 mg/k/day dosage was tolerated through 60 days of exposure. 854

4) Phytotoxicity:

a) Slight phytotoxicity is possible for McIntosh and related (Cortland, Melba, Jonathan, Red and Golden Delicious) varieties of apple and for Rhode Island Greening apple. Has apparently been tested, with safety to the host plants, in control of pests of pear, plum, grape, walnut and citrus fruits, cotton, vegetable field crops and some ornamentals in experimental use. 3204

5) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Chrysops discalis (adult)	Topical	LD_{50} (est.)	65 µg/fly		2707
Chrysops discalis (adult)	Topical	LD_{90}	420 µg/fly		2707
Fannia canicularis (adult) ♀	Topical	LD_{50} 24 hr	0.035 µg/fly	In acetone solution; measured drop test.	1981
Fannia canicularis (adult) ♂	Topical	LD_{50} 24 hr	0.022 µg/fly	In acetone solution; measured drop test.	1981
Musca domestica (adult) ♀	Topical	LD_{50} 24 hr	0.33 µg/fly	In acetone solution; measured drop test.	1981
Musca domestica (adult)	Topical	LD_{50}	16.5 µg/g		2231
Musca domestica (adult) Auburn DDT-R	Topical	LD_{50} 24 hr	0.14(0.1-0.2)µg/fly, 10.52µg/g	Difference not statistically significant.	2110
Musca domestica (adult) Orlando DDT non-R	Topical	LD_{50} 24 hr	0.21(0.19-0.25)µg/fly, 16.89µg/g		2110

b) Comparative toxicities Chlorthion® and other insecticides:

(1) Comparative toxicity for Musca domestica (Auburn strain [DDT-R] and Orlando [DDT-Susceptible strain]; (Auburn = 14 times as resistant to DDT as Orlando); by topical application in acetone solution: 2110

Insecticide	Topical LD_{50} 24 Hrs For			
	Auburn (DDT-R)		Orlando (DDT-Non R)	
	µg/Fly	µg/g	µg/Fly	µg/g
Chlorthion®	0.14 (0.1-0.2)	10.52	0.21 (0.19-0.25)	16.89
Diazinon	0.06 (0.05-0.07)	3.01	0.10 (0.09-0.11)	6.15
Experimental Insecticide 4124	0.03 (0.03-0.03)	2.75	0.02 (0.02-0.03)	1.73
Chlordane	29.0 (12.0-57.0)	2791.3	42.0 (42.0-84.0)	3586.0
Heptachlor	13.0 (11.0-17.0)	855.79	11.0 (8.75-15.0)	955.68
Methoxychlor	2.33(2.03-2.53)	135.18	1.93 (1.33-2.33)	127.49

NB. No significant difference between two strains save in case of Diazinon; note, in others, the overlap of the 0.95% fiducial limits.

(2) Comparative toxicity, Chlorthion® and other insecticides, for Chrysops discalis (adult) by topical application: 2707

Insecticide	LD_{50} (Estimated; µg/fly)	LD_{90} (µg/fly)
Chlorthion®	65	420
Lindane	4	35
Endrin	9	80
DDT	20	250
Dieldrin	20	950
Methoxychlor	30	90
Aldrin	40	170
Heptachlor	40	200
EPN	48	120
Isodrin	60	170
Chlordane	60	650
Diazinon	90	360
3-Chloro-4-methylumbelliferone, O,O-diethyl thiophospate	90	910
Q-137	120	400
Malathion	130	330
Toxaphene	180	480

(3) Comparative toxicity Chlorthion® and other compounds for Musca domestica and Fannia canicularis adults by topical application in acetone by measured drop method; Fannia: Av. Wgt ♂ = 6.89 mg, ♀ = 7.35 mg: 1981

Insecticide	LD_{50} 24 Hrs		
	Musca domestica ♀	Fannia canicularis	
		♀	♂
Chlorthion®	0.33	0.035	0.022
Diazinon	.092	.098	.054

(3) Comparative toxicity Chlorthion® and other compounds for Musca domestica and Fannia canicularis adults, by topical application in acetone by measured drop method; Fannia: Av. Wgt. ♂ = 6.89 mg, ♀ = 7.35 mg: 1981

Insecticide	LD$_{50}$ 24 Hrs		
	Musca domestica ♀	Fannia canicularis	
		♀	♂
Malathion	.56	.10	.06
Pyrethrins	1.0	.24	.44
Dieldrin	.031	.003	.0026
Lindane	.010	.76	.39
Methoxychlor	.068	.14	.12
DDT	.033	2.80	1.30

(4) Comparative toxicity Chlorthion® and other compounds, vs. lice of livestock; vs. Haematopinus eurysternus by spot treatment on cattle; vs. Bovicola caprae and B. limbatus by dips: 2862

Insecticide	Concentration (%)	% Mortality 24, 48 Hrs		Weeks Effective	Degree Of Infestation After 4 Weeks
		Haematopinus	Bovicola	Haematopinus	Bovicola
Chlorthion®	0.002	—	100	—	0
Chlorthion®	.25	100	—	1	—
Parathion	.05	100	—	3	—
Parathion	.01	100	—	3	—
Parathion	.005	25	—	0	—
Malathion	.5	100	—	2	—
Malathion	.25	—	100	—	0
Malathion	.1	—	100	—	0
Malathion	.05	100	100	1	0
Malathion	.025	—	100	—	0
Dipterex	.25	100	—	1	—
Dipterex	.1	100	100	0	light
Dipterex	.05	—	100	—	light
Dipterex	.025	—	100	—	light
Dipterex	.01	—	100	—	light
Dipterex	.002	—	100	—	light
Bayer 21/199	.25	100	—	2	—
Bayer 21/199	.2	100	—	2	—
Bayer 21/199	.1	100	—	1	—
Bayer 21/199	.05	100	—	1	—
Bayer 21/199	.002	—	100	—	0
Bayer 21/200	.002	—	25	—	light
Diazinon	.25	100	—	2	—
Diazinon	.1	100	—	2	—
Diazinon	.05	100	100	1	0
Diazinon	.025	—	100	—	0
Diazinon	.01	95	—	1	—
Diazinon	.005	25	100	1	light
Diazinon	.002	5	—	1	—
Pyrazinon	.25	100	—	3	—
EPN	.05	100	—	1	—
EPN	.01	100	—	1	—
EPN	.005	100	—	1	—
EPN	.002	25	100	0	0
Tetraethyl dithiopyrophosphate	.05	100	—	1	—
DDT	.5	100	—	4	—
DDT	.25	100	100	3	0
Toxaphene	.5	100	—	4	—
Strobane	.5	100	—	4	—
Strobane	.2	—	100	—	0
Strobane	.1	—	100	—	0
Endrin	.05	—	100	—	0
Isodrin	.05	—	100	—	0
2-Pivalyl indanedione	1.0, .5,.25, .1, .05	100	—	2	—

(5) Comparative toxicity Chlorthion® and other substances for certain beneficial insects; as dusts; adult insects placed on plants treated previously by vacuum dusting: 1404

Dust And Concentration		% Mortality 24 Hrs Of		
		Collops vitattus	Hippodamia convergens	Coleomegilla maculata
Chlorthion®	5%	64	82	100
Diazinon	4%	37	66	100
Malathion	5%	47	90	100
Parathion	2%	65	78	98
Dieldrin	2%	36	4	24
Endrin	1%	27	10	18
Toxaphene	10%	32	12	36
Heptachlor	2.5%	41	30	38
Strobane	5%	10	18	12
Perthane	5%	23	6	12
DDT	5%	38	6	32
Control		11	4	0
Lowest Significant Difference (5% Level)		20	24	26

(6) Comparative effectiveness Chlorthion® and other organic phosphate insecticides vs. Anopheline mosquitoes in laboratory and field experiences using acetone solutions in water suspension: 1766

(a) Laboratory tests vs. Anopheles quadrimaculatus (4th instar):

Insecticide	% Mortality 48 Hrs At							
	0.1 ppm	0.05 ppm	0.025 ppm	0.01 ppm	0.005 ppm	0.0025 ppm	0.001 ppm	0.0005 ppm
Chlorthion®	100	—	88	76	44	—	—	—
Sulfotepp	100	—	—	—	—	—	74	34
Parathion	100	—	—	—	—	96	56	34
EPN	100	—	—	—	—	96	32	—
Methyl parathion	100	—	—	—	—	67	—	—
O-(2-Chloro-4-nitrophenyl-O,O-dimethyl thiophosphate	100	—	—	96	86	62	62	44
Malathion	100	—	96	80	80	60	40	24
Ethyl O-nitrophenyl thionobenzene phosphonate	100	—	—	—	70	80	4	—
Diazinon	100	—	—	—	36	20	—	—
Para-oxon	100	—	—	82	50	—	—	—
O-(3-Chloro-4-methylumbelliferone)O,O-dimethyl thiophosphate	100	—	—	64	46	24	—	—
O,O-Diethyl o-piperonyl thiophosphate	100	94	58	26	—	—	—	—
Potasan®	100	98	56	30	.5			
NPD	94	—	62	30	—	—	—	—
DDT (for comparison)	—	—	—	100	94	49	24	—

(b) Field experiences of organic phosphate insecticides vs. Anopheles quadrimaculatus and A. crucians: 1766

Insecticide	% Mortality 24 Hr At Lbs/Acre Shown							
	.25 lbs/acre	.1	.05	.025	.01	.005	.0025	.001
Chlorthion®	100	99	82	73	57	50	—	—
EPN	—	—	95	96	96	95	92	91
O-(3-Chloro-4-methylumbelliferone)O,O-dimethyl thiophosphate	—	—	98	98	99	96	91	84
Parathion	—	—	97	97	92	99	88	—
Methyl parathion	—	100	98	83	69	51	50	—
Ethyl O-nitrophenyl thionobenzene-phosphonate	—	99	80	88	75	70	69	71
Diazinon	—	97	97	79	58	65	55	53
O-(2-Chloro-4-nitrophenyl)O,O-dimethyl thiophosphate	—	99	72	78	49	30	—	—
NPD	100	97	84	87	79	—	—	—
Para-oxon	—	90	77	54	46	45	49	31
Sulfotepp	—	85	72	73	63	53	30	—
Malathion	90	78	79	68	60	—	—	—
O,O-Diethyl O-piperonyl thiophosphate	—	—	78	64	75	74	45	35
Potasan	—	77	59	72	52	—	—	—
DDT (comparison)	—	—	99	98	99	98	95	92

(7) Comparative toxicities Chlorthion® and other organic phosphate insecticides, vs. Musca domestica (after Metcalf): 2231

Insecticide	Topical LD_{50} ($\mu g/g$)
Chlorthion®	16.5
Parathion	0.9
Para-oxon	0.5
Methyl parathion	1.0
Malathion	28
Diazinon	4.6
EPN	1.9
Tetraethyl dithionopyrophosphate	5.0
Tetrapropyl dithionopyrophosphate	15
DFP	15

(8) Test field experiences of Chlorthion® in control of insect pests on an economic scale:

- (a) On vegetable, field crops: At 0.25-0.75 lbs (active)/acre controlled: Aphids, spider mites, flea beetles, cabbage looper, imported cabbage worm. 3204
- (b) On cotton: At 0.3-1.0 lb/acre: Effective vs. boll weevil, leaf hopper; at 0.25-0.5 lb/acre: Effective vs. two-spotted, strawberry, desert spider mites. Long residual effect for cotton leafworm. Initially effective vs. thrips at 0.08 lbs/acre but residual effect no greater than 24 hrs. Ineffective vs. bollworm. 3204
- (c) Vs. Stored products insects: Preliminary tests indicate effectiveness vs. Sitophilus granarius, S. oryzae, Rhizopertha dominica adults in treated wheat grain. Dust incorporated at 4 ppm gave 100% kill S. granarius, S. oryzae; 93% kill Rhizopertha; at 2 ppm gave 100% kill S. oryzae; 77% kill S. granarius; 45% kill Rhizopertha. 2004
- (d) Vs. Tetranychus desertorum (desert spider mite): Compared favorably with Aramite® and Demeton in control of. 2222
- (e) Fly control: Shown to be effective, in 1-2% solutions in sugar baits, to control flies in kitchens, recreation and mess halls, garbage racks and latrines of certain military camps. Promising as a residual wall spray to control, specifically, flies of DDT-R and other chlorinated hydrocarbon-R strains, in barns, pens, farm buildings. Recommended at 4-8 lb (active) per 100 gals water for highly effective long-lasting control, by treatment to run-off of all interior surfaces. Wettable powder formulations appear to be more effective as long-time residues than equal amounts of active ingredient as spray concentrate. No traces in milk of cows from treated dairies; no effect on flavor. 1763 3204
- (f) Mosquito control: Culex tarsalis (DDT-R strains), C. quinquefasciatus, Anopheles quadrimaculatus, A. crucians, Aëdes nigromaculis, were controlled by dosages of 0.2 lbs (active) per acre applied as larvicide. Promise shown vs. adult mosquitoes. 3204
- (g) Household, warehouse pests: Concentrations of 1-2% (active) have shown effective control of Cimex, Sitophilus, Periplaneta, Blattella, Blatta, bean weevil, larder beetle. (Not yet approved for use on stored grains used for food or forage.) 3204
- (h) Cattle insects: Promise shown in preliminary tests vs. Hypoderma spp.

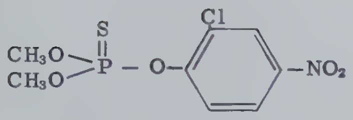
6) Pharmacological, pharmacodynamical, physiological; insects:

a) Consult the general treatment, in this work, of Organic Phosphates.

70

O,O-DIMETHYL O-(2-CHLORO-4-NITROPHENYL) THIOPHOSPHATE

(Dimethyl-2-chloronitrophenyl thiophosphate; Experimental Insecticide 4124, American Cyanamid Co.)



Molecular weight: 297.598

GENERAL

[Refs.: 2120, 2231, 2768, 2803]

An experimental insecticide of recent (1954) introduction and of great promise, as indicated by an elevated toxicity for aphids, effectiveness against Anthonomus grandis and residual insecticidal action. The compound is a quite close relative of parathion, and particularly of such parathion-analogues as methyl parathion, and Chlorthion.® A member of the general class of "organophosphorus" insecticides. For general problems of toxicity, mode of action, pharmacodynamics, etc., consult the general treatment in this work titled Organic Phosphates.

PHYSICAL, CHEMICAL

A white crystalline solid, unstable on prolonged heating at temperatures > 100°C; m.p. (pure compound) 51°C; very low solubility in water; slightly soluble at room temperature in methanol, ethanol, butanol, hexane, heptane, Deobase oil, in all of which, solubility is greatly enhanced by heating; at least 25% solubility in xylene, cyclohexanone, isophorone, ethyl acetate, carbon tetrachloride, diethyl succinate, amyl acetate, toluene, methyl isobutyl ketone; at least 10% solubility in polyethylene glycol 400, ethyl cellosolve; very soluble in acetone. Emulsifiable liquids may be prepared using 5-10% emulsifier and aromatic solvents, e.g. xylene.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse, Rat ♂♂♀♀	or	LD_{50}	470-650	As 10% solution in Wesson oil.	2803
Mouse ♂	or	LD_{50}	1350	As 10% solution in propylene glycol.	2803
Rat ♂	or	LD_{50}	1310	As 10% solution in propylene glycol.	2803
Rat ♂	or	LD_{50}	1710(1260-2330)	10%, 20% water suspensions.	2803
Rat	or	LD_{100}	200		2768
Rat ♂	or	LD_{50}	1710	As suspensions in water, methyl cellulose.	2803
Mouse	or	LD_{50}	400	Compare with 31.5 mg/k for diethyl-analogue.	2120

a) Dog: Single oral dose in corn oil, 200 mg/k, yielded gross symptoms, cholinesterase inhibition; animals survived. 2803

b) Guinea Pig: Single dry applications to skin (exposures of 18 hrs) as high as 2000 mg/k gave no adverse effects, no evidence of cholinesterase inhibition; animals remained in good health throughout 2 weeks. At autopsy: No significant gross pathology. Compound not readily absorbed via skin in the dry form.

c) Rabbit: 50% solution (Wesson oil), 0.1 cc instillation to conjunctival sac gave slight irritation only; light response of pupil was not affected; 2nd application 2 hrs later yielded no effect. 2803

d) Vapor hazard:

(1) Normal volatilization at room temperature presents no hazard because of a vapor pressure too low to permit building up of dangerous concentrations. 2803

2) Subacute, chronic toxicities; repeated dosage effects:

a) Rats:

(1) At 4 successive doses, 200 mg/k, 1 dose/day, oral (10% in Wesson oil) 7 of 7 animals died. 2803

(2) At concentrations of more than 1000 ppm (= daily intake 100 mg/day) lethal within 1 week. 3 of 5 animals died within week at 500 ppm.

(3) On diets containing 25, 100, 250 ppm, 54 weeks exposure: No deaths, no systemic intoxication signs. Cholinesterase activity not determined.

(4) 4 groups (♂♂, 20/group) 54 weeks exposure to 0, 25, 100, 250 ppm in diet (as a 10% dust): No deaths attributable to insecticide; food consumption comparable to controls; growth rate slightly (not significantly) less than controls at 25 ppm; at 100 ppm significant growth retardation; even more accentuated at 250 ppm. At autopsy ("sacrifice");* No significant gross pathological changes. Mean daily intake at 25 ppm = 2 mg/k; at 100 ppm = 7 mg/k; at 250 ppm = 18 mg/k.

(5) ♂♂, 5/group, exposed to 0, 100, 500, 1000, 5000, 10,000 ppm: All on 1000, 5000, 10,000 ppm dead within 1 week; 3 of 5 at 500 ppm dead within 1 week. Before death all showed: Tremors, salivation followed by depression; inanition was a possible minor factor in deaths at the higher feeding levels. Controls and animals on 100 ppm for 7 weeks showed at autopsy ("sacrifice") no significant gross pathology.

* The use of words like this one in such a context grows increasingly noxious to those who respect the English tongue.

b) Dogs: 2803

(1) 6 (3♀♀, 3♂♂) 2/group (1♂, 1♀), repeated doses at 10, 50, 100 mg/k daily dosage 6 days/week, total of 18 or 31 doses: Progressive decrease in plasma and erythrocyte cholinesterase activity. In 2 weeks, following dose 31, plasma cholinesterase returned virtually to control level; brain cholinesterase showed but slight recovery. At 10 mg/k/day (31 doses in 36 days): ♂ gave no signs systemic toxicity save slight weight loss; ♀ showed after dose 11: Salivation, slight ataxia, dyspnoea of short duration and not later observed again; autopsied 14 days after dose 31 showed no significant gross pathological changes; brain cholinesterase activity significantly reduced. At 50 mg/k/day: ♂ , 31 doses over 36 days: After dose 6 gross toxic signs: Salivation, ataxia. Depression, ataxia, dyspnoea, loose stools recurrent at intervals. After dose 31 animal alert, good appetite, but excreting soft stools. ♀ after 16 doses in 18 days yielded severe toxic symptoms; experiment ended. At 100 mg/k/day (16 doses in 18 days): ♂ after dose 4 showed excessive salivation; after dose 5 showed ataxia, fasciculation, dyspnoea, over-excitability clearing overnight and not recurring after dose 6. In second week: Salivation, dyspnoea, ataxia following each dose, but clearing overnight. In the ♀ similar signs. Recovery after discontinuance with normal appearance, behavior, appetite, reversal of weight loss in 4 weeks observation after end of experiment. At end of 4 weeks plasma cholinesterase was at control level; erythrocyte cholinesterase ♂ 15%, ♀ 50% of control level. At "sacrifice", brain cholinesterase normal.

3) Pharmacological, pharmacodynamical, physiological etc.:

a) The foregoing data suggest the mode of toxic action as an inhibition of acetylcholine esterase activity, with the attendant signs of this effect. (See the general treatment of Organic Phosphates)

b) In summary:

(1) In rats, oral doses at 200 mg/k, repeated doses: Tremors, excessive lacrimation within 1 hour after dose 1; within 3 hours, 7 of 7 animals comatose. After dose 2, 2 deaths in several hours, followed later by 2 more deaths; no survivors after dose 4. 2803

(2) Following single 200 mg/k oral doses to ♂ white rats: Plasma and erythrocyte cholinesterase activity declined to 10% normal in 24 hours. Plasma esterase was restored quite rapidly to control levels within 7 days; erythrocyte esterase activity ca. 80% control value at 28 days after single 200 mg/k dose.

(3) At the LD_{50} level (1.71 (1.26-2.33) g/k) rats excreted a deep yellow urine. At higher dosage levels survivors exhibited (for 2-3 days after dosage) excessive cholinergic activity. Gross autopsy of animals dead at LD_{50}: Signs of irritation of gastrointestinal, peritoneal mucous surfaces. No significant pathological signs in survivors autopsied at end of 8 day observation.

(4) In dogs (2 animals 1 ♀, 1♂): After single oral dosages of 200 mg/k, plasma and erythrocyte cholinesterase activity was much depressed, with plasma activity initially more markedly affected than red cell activity. Plasma activity recovered more rapidly to control levels in 7 week period; at end of 7 weeks erythrocyte cholinesterase activity was still significantly below normal. Soft feces (in ♀), vomiting, diarrhoea (in ♂) following the single dosage were noted. At autopsy ("sacrifice") 47 days and 49 days later brain cholinesterase was found normal.

4) Toxicity for insects:

a) Quantitative

Insect	Route	Dose	Dosage	Remarks	
Aphids (sp??)	?	LC_{90}+	1:28,000	In aqueous solution.	2120
Mosquitoes (culicine larvae)	Medium	LC_{50}	0.017 ppm		2803
Mosquitoes (culicine larvae)	Medium	LC_{90}	0.029 ppm		2803
Musca domestica Auburn DDT-R	Topical	LD_{50} 24 hr.	0:03 μg/fly, 2.75 μg/g	No significant difference.	2251
Musca domestica Orlando DDT-non R	Topical	LD_{50} 24 hr.	0:02(0.02-0.03) μg/fly (1.73 μg/g)		2251 2803

b) Comparative toxicity, Experimental Insecticide 4124 and other compounds for larvae of mosquitoes (culicine). 2803

Insecticide	LC_{50} (ppm)	LC_{90} (ppm)
Exp. Insect. 4124	0.017	0.029
Malathion	.13	.23
Exp. Insect. 12008	.027	.08

(1) Tests of residual activity for Musca domestica (adults), exposed to wooden panels sprayed with 2% (ca) emulsions of 25% concentrates at 60 mg/ft²:

Time After Spraying Weeks	% Mortality With			
	4124	Malathion	Chlorthion	Diazinon
0	100	99	76	100
1	100	57 (?)	5 (?)	100

(1) Tests of residual activity for Musca domestica (adults), exposed to wooden panels sprayed with 2% (ca) emulsions of 25% concentrates at 60 mg/ft^2.

Time After Spraying Weeks	% Mortality With			
	4124	Malathion	Chlorthion	Diazinon
2	99	78	39	96
3	100	87	12	68
4	79	48	0	29
5	62	13	0	8

(2) Tests (as above) vs. Musca domestica, but with sugar (10%) added to the 2% emulsion. Greenhouse tests with panels aged rapidly in drafts of air from fans. Panels treated in spray tower and aged in greenhouse:

Days After Spraying	% Mortality With	
	4124	Malathion
0	100	95
2	100	30
11	100	19
30	100	—
35	26	—

(3) Residual toxicity of 4124 and other compounds on panels, treated by dipping in 1% concentrations, with and without 12% sugar. Musca domestica (adult; in 10 in × 10 in × 10 in cages) exposed to treated panels aged 6 and 13 weeks after treatment:

Insecticide		% Insects Down After				
		2 hrs	4 hrs	2 hrs	4 hrs	20 hrs
		(Panels Aged 6 Wks)		(Panels Aged 13 Wks)		
4124	1%	0	0	0	0	14
4124	1% + 12% sugar	21	44	47	72	89
Malathion	1%	0	0	1	3	4
Malathion	1% + 12% sugar	12	68	21	51	80
Chlorthion	1% (wett. pwdr.)	0	2	0	0	2
Chlorthion	1% (wett. pwdr.) + 12% sugar	0	0	0	1	9

c) Fly control by Experimental Insecticide 4124 in field tests as a residual spray, 1954, chiefly in dairy barns in various parts of the U.S.: 2803

(1) Summary statement: Used mainly as 1% sprays (in some instances as 0.5, 2 1/2% sprays), with and without sugar or added syrup, control ranging from 2-8 + weeks duration has been recorded. The evaluation is said to have been rather inconclusive because of generally low fly "populations" due to a relatively dry season.

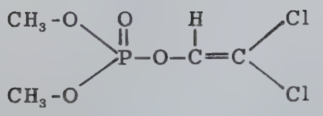
(2) Stated to be effective, and with good residual action, against Anthonomus grandis (Cotton boll weevil). 2120

d) Screening tests indicate high activity vs. lice (insecticidal, KD), mosquitoes (as larvicide) and as a space spray for flies. 1801

71

DIMETHYL 2,2-DICHLOROVINYL PHOSPHATE ("DDVP"; O,O-Dimethyl-O-2,2-dichlorovinyl phosphate)

$C_4H_7O_4PCl_2$



Molecular weight: 227

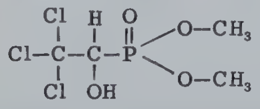
GENERAL 2140

An organophosphorus insecticide of high toxicity to insects. As an experimental insecticide dimethyl 2,2-dichlorovinyl phosphate has shown particular promise as a space spray, and in bait formulations, for control of flies. The toxicity of "DDVP" for *Musca domestica* is approximately equal to the toxicity of parathion, but for the albino rat it is from 5-10 times less toxic than parathion.

a) The toxicological margin of safety leaves something to be desired.

PHYSICAL, CHEMICAL

1) Discovered as an impurity, highly toxic to *Musca domestica*, in O,O-dimethyl 2,2,2-trichloro-1-hydroxyethyl phosphonate (Dipterex®; Bayer L 13/59) q.v., whose formula is: 2140



   a) Dehalogenation of Dipterex® with alkali yields a product insecticidally equivalent to the observed impurity.
   b) The structural formula of "DDVP" shows that dehalogenation is accompanied by rearrangement to yield dimethyl 2,2-dichlorovinyl phosphate.
   c) "DDVP" as an impurity in technical Dipterex® is present to ca 0.03%, and being volatile disappears progressively from aerated Dipterex®.

2) Addition of 1 mole NaOH to 1 mole O,O-dimethyl 2,2,2-trichloro-1-hydroxyethyl phosphonate in water yields an oily material which separates and which has the biological properties of the observed impurity.
   a) The oily liquid is "DDVP", which is indicated to be:
      (1) Heat sensitive,
      (2) Soluble in ether and presumably other organic solvents,
      (3) Volatile.
   b) The degradation of Dipterex® to "DDVP" is summarized as the loss of 1 chlorine atom, and probably 1 hydrogen atom, with the dechlorination probably the major change.

TOXICOLOGICAL 2140

1) Toxicity for higher animals:
   a) Comparative toxicity of "DDVP", parathion, Dipterex®, for albino rats.
   *C 19/20 L = Confidence (19/20) Limits.

Route		"DDVP" (pure)		Parathion (tech)		Dipterex® (tech)	
		LD_{50}	C 19/20L*	LD_{50}	C 19/20 L	LD_{50}	C 10/20 L
					(mg/k)		
Dermal (in xylol)	♀	75	(59- 96)	10.9	(7.89-12.93)	—	—
	♂	107	(84-137)	21.0	(14-34)	—	—
Oral (in peanut oil by stomach tube)	♀	56	(48- 65)	3.6	(3.2 - 4.0)		
	♂	80	(62-104)	13.0	(10.2-16.5)	630 (in H_2O)	(568-699)

   (1) "DDVP" is thus 5-10 times less toxic than parathion to the rat, and ca. 10 times more toxic than Dipterex®.

   (2) Toxicity of a related ester, diethyl 2-chlorovinyl phosphate: Appears to be considerably more toxic than "DDVP" for mammals. 600

2) Toxicity for insects:

a) Comparative toxicity for Musca domestica, topical application: 2140

Compound		Approximate LD_{50} (μg/insect)
Dipterex®	(tech)	0.2
"DDVP"	(tech)	0.03
"DDVP"	(pure)	0.022
Parathion	(tech)	0.023

(1) The ethylester is insecticidal with an LD_{50} topical of ca 0.1 μg/fly.

(2) Diethyl 2-chlorovinyl phosphate is also insecticidal, the LD_{50}, topical, of the tech. product being ca 0.1 μg/fly, but more toxic to rats than "DDVP". 600

(3) It is suggested that dimethyl 2-chlorovinyl phosphate may be more toxic for insects. 2140

b) Tested in poison baits, 0.1% and 0.01% in 10% sugar solutions, sprayed as liquid in milking barns, "DDVP" in Georgia dairy experiments gave the following results: 1795

(1) Spectacular, immediate decrease of house flies; grill counts dropping from 233 to 3 at 3 hrs. after application.

(2) In calf pens the average index dropped from 2000 to 7 flies, but the density rose, in some cases, again to undesirable levels in 48 hrs and in other cases after 3-5 days with 0.1% formulations. Immediate results with 0.01% formulations satisfactory, but the effect was gone within less than 24 hrs.

(3) It was concluded from these experiments that "DDVP" has promise as a practical toxic bait for Musca but (like malathion, Dipterex®, diazinon) frequent applications are necessary to maintain low fly densities.

3) A comparison of the absorption and translocation of P^{32} labelled, radioactive DDVP and Dipterex® (it is to be recalled that DDVP is a dehydrochlorination product of Dipterex®) in Periplaneta americana: 7

a) Both DDVP and Dipterex® are readily absorbed by Periplaneta via topical application to the cervical membrane.

b) DDVP is far more toxic to Periplaneta than is Dipterex® and only very small amounts can be used.

c) In the case of Dipterex® radioactivity was widespread in the tissues and the haemolymph, with most of the radioactivity concentrated, after 20 hours, in the gut.

d) By contrast with the above, DDVP treated Periplaneta showed no haemolymph radioactivity (the minuteness of the dose must be considered), and many other tissues showed but slight radioactivity. Much radioactivity was concentrated in heart tissue shortly after application, while after 22 hours most was concentrated in the fat body, with only a small amount in the gut. The conclusion follows that DDVP is very rapidly segregated from the haemolymph by the tissues of Periplaneta.

4) Toxicity and mode of action of some chlorinated organic phosphates, relatives of DDVP, of the general formula 2285

$(R\text{-}O)_2 = \overset{O}{P}\text{—}O\text{-}CHClCCl_3$, tested against Musca domestica (Orlando-Beltsville, DDT-R biotype subjected to 150 generations of selection vs. DDT and the NAIDM, DDT-non R biotype). Anti-choline esterase activity, expressed as ID_{50} (30 minutes), the molar concentration yielding 50% inhibition in 30 minutes, in vitro, tested against bovine erythrocyte choline esterase:

Ester	DDT-non R, NAIDM Biotype		DDT-R, Orlando Biotype		ID_{50} (30 min)	Inhibition
	Topical LD_{50} (μg/fly)	Toxicity Ratio	Topical LD_{50} (μg/fly)	Toxicity Ratio	Bovine Erythrocyte ChE	Ratio
Dimethyl	0.123±.005; .140±.006; .154±.016	1	0.217±.010; 0.233±.012	1	8.24×10^{-7} M	1
Diethyl	0.164±0.009	0.75 ±.041	0.257±.016	0.844±.066	6.93×10^{-8} M	11.89
Dipropyl	0.343±0.010	0.359±.034	1.36 ±.027	0.160±.010	2.25×10^{-7} M	3.67
Di-isopropyl	0.774±0.032	0.181±.012	0.294±.056	0.793±.154	7.0×10^{-2} M	1.24×10^{-5}
Dibutyl	0.596±0.060	0.261±.038	1.22 ±.068	0.191±.014	9.5×10^{-6} M	8.7×10^{-2}

a) Correlation appears between chemical structure and toxicity to Musca.

b) Toxicity to DDT-non R biotype declines with increase in carbon chain length of the alkyl group with diethyl, dipropyl, dibutyl being respectively 0.75, 0.36, 0.26 as toxic as dimethyl with di-isopropyl being the least toxic.

c) Toxicity toward DDT-R biotype: Diethyl, dipropyl, di-isopropyl, dibutyl are respectively 0.75, 0.16, 0.79, 0.19 as toxic as the dimethyl ester.

d) No correlation shown between choline esterase inhibition and chemical structure; all inhibited bovine erythrocyte Ch E.

e) DDT-R Musca showed only a slightly greater tolerance for these compounds than did the non-R biotype.

5) Residues:*

a) An enzymatic method, elaborated for the determination of Demeton residues, has been adapted for DDVP on such fruits as guava, mango, avocado, various Citrus. The method has been tested, also, to determine residues on Lima bean, Coleus and Geranium plants.

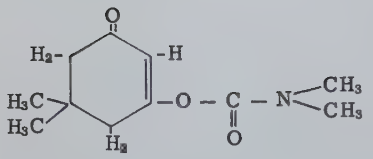
(1) The foregoing follows on the suggested use of DDVP vs. oriental fruit and melon flies.

(2) The method, sensitive to 0.5 μg of DDVP, reveals the virtual disappearance of residues after 72 hrs.

* Data noted too late to be included in Bibliography derives from: Giang, P.A., et al., Journal of Agricultural and Food Chemistry 4 (7): 621, 1956.

72

5,5-DIMETHYLDIHYDRORESORCINOL DIMETHYLCARBAMATE (Dimetan; G-19258 [Geigy.]; Dimethyl dihydroresorcinol dimethylcarbamate.)



Molecular weight: 211.254

GENERAL

[Refs.: 3271, 2231, 1317, 1316, 1120, 1134, 1386, 1286, 2942]

An insecticide of recent (1951) introduction which has shown itself to be an aphicide of high potency, and a specific acaricide (vs. Bryobia). Dimetan shows a high order of systemic activity as well as a high degree of contact toxicity for insects. Dimetan is a member of the general class of carbamate insecticides (see the general treatment in this work titled Carbamates, etc.). Other members of the class (Isolan, Pyrolan, Pyramat) may also be found in this work. These compounds show a swift action against flies which resembles that of pyrethrins. Ineffective vs. red spider mites.

PHYSICAL, CHEMICAL

Technical: A yellow crystalline solid; pure: Whitish crystalline solid; m.p. 45°-46°C; b.p.: Volatile in steam; soluble in water to the extent of 3.15% at 20°C; moderately soluble in petroleum oils; soluble to a limited extent in numerous organic solvents.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks
Mouse	or	LD_{50}	90	Pyrolan LD_{50} = 62 mg/k. 1119, 1120, 1134
Mouse	iv	LD_{50}	12.5	1120, 1134
Rat	or	LD_{50}	150	Pyrolan LD_{50} = 90 mg/k. 1119, 1120, 1134
Dog	or	LD_{50}	50	1120, 1134

2) Chronic and sub-acute toxicity for higher animals:
   a) Mouse: 10 mg/k/day in the diet yielded fatty infiltration of the liver; 25 mg/k/day showed fatty infiltration of kidneys. 1120
   b) Rat: 10-100 mg/k/day gave no observable pathological changes; such dosage levels were tolerated. 1120
   c) Absorption via the skin is negligible. 1120

3) Pharmacological, pharmacodynamical, physiological, etc.
   a) Consult the general treatment of Carbamates, etc. in this work.

4) Phytotoxicity:
   a) Experiences indicating the systemic insecticidal activity of Dimetan in treated plants, would suggest that in some plants at least, it may exist at insecticidal levels without damage. 1286

5) Toxicity for insects:
   a) Quantitative:

Insect	Route	Dose	Dosage	Remarks
Aphis rumicis	or	LD_{50}	.0005 μg/insect, 0.8 μg/g	1119, 1286
Aphis rumicis	or	LD_{100}	.001 μg/insect, 1.6 μg/g	1119, 1286
Apis mellifera (adult)	or	LD_{50}	1.5 μg/insect, 13 μg/g	1119, 1286
Apis mellifera (adult)	or	LD_{100}	2.0 μg/insect, 18 μg/g	1119, 1286
Ceratitis capitata	or	LD_{50}	92 μg/g	Insect cholinesterase $I_{50}=5.6\times10^{-7}$ M. 2659
Deltocephalus cucurbitae	or	LD_{50}	128 μg/g	Insect cholinesterase $I_{50}=6.5\times10^{-7}$ M. 2659
Deltocephalus dorsalis	or	LD_{50}	117 μg/g	Insect cholinesterase $I_{50}=5\times10^{-7}$ M. 2659
Ephestia kuehniella	or	LD_{50}	0.5 μg/g, .005 μg/insect	1119, 1286
Ephestia kuehniella	or	LD_{100}	.0075-.01 μg/insect, .7-.75 μg/g	1119, 1286

a) Quantitative:

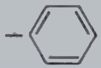
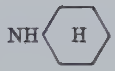
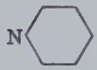
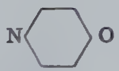
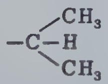
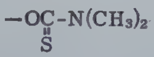
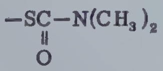
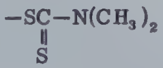
Insect	Route	Dose	Dosage	Remarks
Musca domestica	or	LD_{50}	.05-.07 μg/insect, 3.2 μg/g	1848, 1119, 1286
Musca domestica	or	LD_{100}	.3 -.4 μg/insect, 27 μg/g	1119, 1286
Plusia gamma	or	LD_{50}	10 μg/insect, 30 μg/g	1119, 1286
Plusia gamma	or	LD_{100}	12-18 μg/insect, 36-54 μg/g	1119, 1286

Also consult Ref. 3273.

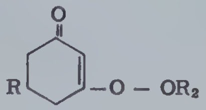
b) Comparative toxicity Dimetan and other compounds for insects: 1119, 1286

Insect	Dimetan				Pyrolan				Parathion	
	LD_{50}		LD_{100}		LD_{50}		LD_{100}		LD_{50}	
	(μg/insect)	(μg/g)	(μg/insect)	(μg/g)	(μg/insect)	(μg/g)	(μg/insect)	(μg/g)	(μg/insect)	(μg/g)
Plusia gamma	10	30	(12-18)	36-54	8	24	(10-12)	30	2.5	7.5
Apis mellifera	1.5	13	2	18	(1.0-1.5)	13	2	18	0.1	1.0
Musca domestica	(.05-.07)	3.2	(.3-.4)	27	(.05-.07)	3.2	(.3-.4)	27	.01	.5
Ephestia kühniella	.005	.5	(.01-.0075)	(.7-.75)	.005	.5	.0075	.7	.01	1.0
Aphis rumicis	.0005	.8	.001	1.6	.0005	.8	.001	1.6	.0005	.8

c) Chemical structure and insect toxicity: 1317

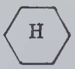
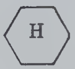
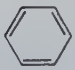
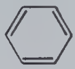
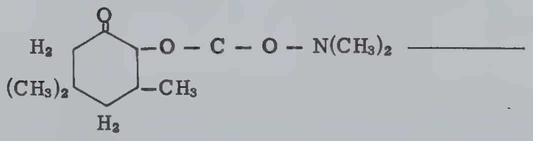
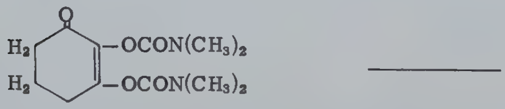
Designation	Substituent $-N\begin{smallmatrix}R_1\\R_2\end{smallmatrix}$	Dosage Toxic To Musca As A Deposit (mg/cm^2)
Dimetan (G-19258)	CH_3-, CH_3-	0.01-0.1
G-21912	CH_3-, C_2H_5-	10
G-19255	CH_3-, C_4H_9-	10
G-54	C_2H_5-, C_2H_5-	1 — 10
G-22055	C_3H_5-, C_3H_5-	—
G-21918	C_3H_7-, C_3H_7-	10
G-19018	C_4H_9-, C_4H_9-	10
	(Replacement of $-N\begin{smallmatrix}R_1\\R_2\end{smallmatrix}$ by)	
G-22062		10
G-19256		1 —10
G-19254		1 —10
G-19257		No activity
G-21906	 $-C(H)\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}$	No activity
	(Replacement of Oxygen of carbamate portion of molecule by S)	
G-22455	 $-O\overset{}{\underset{\|\atop S}{C}}-N(CH_3)_2$	1
G-22441	 $-S\underset{\|\atop O}{C}-N(CH_3)_2$	1
G-22381	 $-S\underset{\|\atop S}{C}-N(CH_3)_2$	No activity

Activity For Musca Of Products Of Type

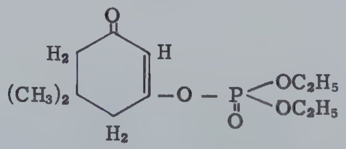


Designation	R_1	R_2	Toxicity For Musca As Deposit (mg/cm^2)
G-21560	H	$-N(CH_3)_2$	1
G-21921	H	$-N\begin{smallmatrix}CH_3\\C_2H_5\end{smallmatrix}$	1
G-21544	H	$-N(C_2H_5)_2$	10
G-22051	H	$-N\begin{smallmatrix}CH_3\\C_4H_9\end{smallmatrix}$	10

Activity For Musca Of Products Of Type

Designation	R_1	R_2	Toxicity For Musca As Deposit (mg/cm²)
G-22161	H	$-N(C_3H_5)_2$	10
G-21919	H	$-N(C_4H_9)_2$	10
G-21910	CH_3	$-N(CH_3)_2$	0.1
G-21907	CH_3	$-N\begin{matrix}CH_3\\C_2H_5\end{matrix}$	1
G-21909	CH_3	$-N(C_2H_5)_2$	10
G-21908	CH_3	$-N(C_4H_9)_2$	> 10
G-21911	CH_3	$-N(C_4H_9\ iso)_3$	> 10
G-22006	$\begin{matrix}CH_3\\CH_3\end{matrix}>CH$	$-N(CH_3)_2$	1
G-22057		$-N(CH_3)_2$	No activity
G-22058		$-N(C_2H_5)_2$	> 10
G-22002		$-N(CH_3)_2$	10
G-21545		$-N(C_2H_5)_2$	10
			1
			10

(1) The dimethylurethanes are the most active members of the series. 1317
(2) The diethyl analogue of Dimetan has repellent activity for flies, but little insecticidal activity. 1317
(3) Replacement of the dimethylcarbamate by the diethyl ester of phosphoric acid to give: 1317

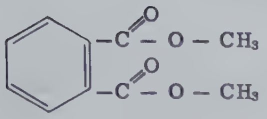


results in a compound of powerful insecticidal action.

6) Pharmacological, pharmacodynamical, physiological, etc., insects:
   a) Consult the general treatment in this work Carbamates, etc.
      (1) The mode of action in the insect body of Dimetan and Pyrolan is apparently similar. 1119, 1286
      (2) Applied to the thoracic ganglion of Periplaneta americana tremors of the extremities result. The action is central in the ganglionic motor elements, and not distal on the peripheral nerves. During the tremors the respiratory rate increases sharply; blood pH and muscle pH pass to the acid level; lactic acid rises and death by auto-intoxication may be postulated. Anti-cholinesterase action is intense, especially for Pyrolan.
   b) Killing action is rapid with Dimetan against aphids; 90% mortality with lethal doses was obtained in the first 20 minutes, 98% mortality within 1 hour. The action of Pyrolan was slower, but the final mortality achieved was equal to that caused by Dimetan. Both substances are powerfully aphicidal. Both show systemic action, which is modified, in degree and extent, by physical variables of temperature, humidity, etc.

73

DIMETHYL PHTHALATE (DMP; Methyl phthalate; Dimethylbenzene orthodicarboxylate)



Molecular weight: 194.18

GENERAL

(Also consult dibutyl phthalate, dibutyl adipate)
[Refs.: 774, 2120, 353, 2600, 1804, 3116]

An insect repellent whose properties were first reported in 1929. Used for a long time as a standard insect skin repellent for military forces, combined with Indalone (n-butyl mesityloxide oxalate) q.v., and Rutgers 612 (2-ethyl-1,3-hexanediol) q.v., in the proportions 6 : 2 : 2, and for this reason commonly called 6-2-2. Intensive investigation of repellency in recent years resulted in the replacement of the latter formulation (not fully satisfactory in meeting military requirements for an insect skin repellent) by a new formulation which has become standard: DMP 40%, Rutgers 612 30%, dimethyl carbate (dimethyl ester of cisbicyclo (2,2,1)-5-heptene-2,3-dicarboxylic acid) 30%, a mixture which is repellent for anopheline mosquitoes for 2 hours per application and for 4 hours per application vs. Aëdes spp., ticks, chiggers, and various trombiculid mites. DMP has also shown some acaricidal effectiveness. The vapors of DMP are said to be sufficiently toxic to kill Periplaneta americana.

DMP is recommended as an insect repellent for direct application to the body by its lack of adverse effect on the skin.

PHYSICAL, CHEMICAL

An aromatic ester; colorless—yellowish, viscous liquid; b.p. 285°C; $d^{25°}_{25°}$ 1.189; $n^{20°}_{D}$ 1.5168; v.p. at 20°C 0.01 mm Hg, at 150°C 12.5 mm Hg; volatility $>$4 mg/cm^2/hour at 100°C; virtually insoluble (0.43% w/w) in water; practically insoluble in mineral oils, miscible with alcohols, ether and many organic solvents; chemically stable but subject to hydrolysis in alkaline media.
Formulation: May be used as such or (as indicated above) in various mixtures or combined with creams, lotions, etc.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage	
Mouse	or	LD_{50}	7.2 cc/k	842
Mouse	sc	MLD	ca 6000 mg/k	931
Mouse	ip	LD_{50}	3640 mg/k	1748
Rat	or	LD_{50}	6.9 cc/k	842
Guinea Pig	or	LD_{50}	2.4 cc/k	842
Rabbit	or	LD_{50}	4.4 cc/k	842
Chicken	or	LD_{50}	8.5 cc/k	842

2) Chronic and subacute toxicity:
   a) The hazard for chronic toxicity, when properly used, appears to be negligible.
   b) Use of DMP entails no serious or adverse effects for human skin. DMP is irritating to the eyes and mucous membranes. 1804, 3116

3) Effects upon insects and acarines: 1801
   a) Extensive screening tests may be summarized as follows:
      (1) DMP is ineffective as an insecticide or "knockdown" agent, vs. Pediculus humanus corporis and has an initial but evanescent effect as a louse ovicide.
      (2) Vs. mosquito larvae (Anopheles quadrimaculatus) DMP fell into the class of lowest effectiveness; less than 50% kill 24, 48 hours at 10 ppm.
      (3) Vs. trombiculids (Trombicula splendens, T. alfreddugesi), in the "cloth patch test," DMP served as an effective initial toxicant, but proved ineffective after a 15 minute rinse of the treated cloth; in "knockdown" tests on cloth patches, DMP showed complete "knockdown" of test chiggers in 1-5 minutes.
      (4) As a skin and clothing repellent for Anopheles quadrimaculatus, Aëdes aegypti A. taeniorhynchus, A. sollicitans, DMP showed: 180 minutes protection time per application for Aëdes spp., 90 minutes

protection time per application from bites of *Anophelus quadrimaculatus*. As an impregnant for clothing DMP effectively repelled for periods of more than 21 days *Aëdes aegypti*, *Anopheles quadrimaculatus*, and was effective for 6-10 days vs. *Aëdes taeniorhynchus*, *A. sollicitans*. Skin protection time for "salt-marsh" mosquitoes (*A. taeniorhynchus*, *A. sollicitans*) was somewhat less than for others.

(5) In wearing tests of impregnated clothing, DMP showed itself of rather low effectiveness giving 0-8 hours protection from *Aëdes aegypti* and 16-24 hours protection from the other above-mentioned mosquitoes.

(6) In washing tests of impregnated cloth, repellency of DMP did not survive a single rinsing of 15 minutes in cool water when tested against *A. aegypti*, *A. quadrimaculatus*.

(7) As a flea repellent and tick repellent ("patch tests" with *Ctenocephalides felis, Xenopsylla cheopis, Amblyomma americanum*) DMP was ineffective after the first day for fleas and effective for 1-5 days for ticks.

(8) Some degree of synergism with pyrethrins vs. lice was demonstrated.

b) Protection time with DMP is strongly affected (adversely) by dry heat; change from 80°F (dry bulb), 70°F (wet bulb) to 90°F (dry bulb) 70°F (wet bulb) dropped protection time from 267 minutes to 99 minutes. Little additional decrease of protection time shown with increasing relative humidity (change from 90°F (dry bulb) 70°F (wet bulb) to 90°F (dry bulb), 80°F (wet bulb)). 2508 2509

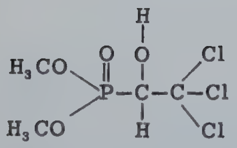
c) The temperature of the host is important in repellency duration time as are, also, absorption by the skin, dilution by sweat, chemical interaction and alteration of the repellent in contact with skin.

d) DMP has shown repellent action for greenhouse thrips. 2691

e) Critical studies indicate a direct action on the chemosensory systems of insects by true repellents. *Musca*, *Stomoxys*, *Glossina*, *Phormia* deprived of antennae and other sense structures, no longer avoided vapor repellents. Progressive extirpation of the chemosensory organs was correlated with a steadily increasing rise in the concentration of repellent needed to repel. 774

74

O,O-DIMETHYL-2, 2, 2-TRICHLORO-1-HYDROXYETHYL PHOSPHONATE (Dipterex®; Bayer L 13/59; Dimethyltrichlorohydroxyethyl phosphonate; O,O-Dimethyl 1-hydroxy-2-trichloromethyl phosphonate; Dimethyl ester of 2, 2, 2-trichloro-1-hydroxyethyl phosphonate.)



Molecular weight: 257.454

GENERAL [Refs.: 3204, 2231, 2120]

An "organophosphorus" insecticide, introduced in 1952 for experimental use. Dipterex® has proved itself in use as a highly effective insecticide for baits employed to control *Musca domestica* and other flies. The "knockdown" is very rapid with Dipterex® and high effectiveness in controlling flies in dairy and livestock barns, milk processing and holding rooms, poultry houses, pig pens, garbage accumulations, manure piles, etc., has been shown. Dipterex® has shown promise against lepidopterous and dipterous insects, (adults, larvae), and mites on fruit, vegetable and field crops, against mosquito larvae, household pests, particularly chlorinated-hydrocarbon-R cockroach strains. Experimental promise vs. such internal insect parasites of cattle as *Hypoderma* spp. has been noted. Mammalian toxicity is relatively low and offers a good margin of safety. Consult also the general treatment of Organic Phosphates in this work for data of common interest to this whole class of toxicants.

PHYSICAL, CHEMICAL [Refs.: 3204, 2231, 2120, 2141, 196]

A solid, white to pale yellow, crystalline, of pleasant odour; m.p. 83°-84°C [3204], 78°-80°C [2120, 2231] b.p. at 0.05 mm Hg 91°C, at 0.1 mm Hg 100°C, at 0.2 mm Hg 109°C, at 0.4 mm Hg 120°C; $d_4^{20^\circ}$ 1.73; $n_D^{20^\circ}$ (10% aqueous solution) 1.3439; volatility: At 20°C = ca 0.1 mg/m³, at 40°C = ca 2.0 mg/m_3; soluble in water to 13-15% at 25°C; soluble in alcohols, diethyl ether, benzene, toluene, ligroin, and in most chlorinated hydrocarbon solvents such as methylene and ethylene chlorides, chloroform; slightly soluble in petroleum ether, carbon tetrachloride; stable at room temperature in neutral or slightly acid media; slow decomposition on long standing in aqueous solution, the solution becoming acid; decomposition speeded by heat; unstable in alkaline media, being converted by mild alkali to water—insoluble, highly toxic O,O-dimethyl O-2,2-dichlorovinyl phosphate, q.v. Incompatible with Bordeaux mixture, lime-sulfur, lime, or any material yielding a pH > 7.5, in spray mixtures. Presumably compatible with other pesticides.

Formulation: (high solubility in water provides an unusual advantage) as 50% soluble powder; 5, 10% dusts; Dipterex® tablets; 1% sugar baits; Dipterex® fly discs ("Tugon Fly Mat"); Dipterex® Technical (available for special purposes from the manufacturers). Hazardous if swallowed, inhaled or absorbed via skin; contact, prolonged inhalation of dusts and spray mists, contamination of food and forage to be avoided. Direct contact of animals to be guarded against; areas of buildings, barns, etc., which animals may lick should not be treated; treated garbage is not suitable for animal food. Surfaces treated with lime, whitewash, or alkaline coatings are not to be treated with Dipterex®.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	
Rat	or	LD_{50}	450	862
Rat	or	LD_{50}	500	748
Rat	ip	LD_{50}	225	862
Mouse	or	LD_{50}	500	2120
Guinea Pig	or	LD_{50}	300	2120
Rabbit	ct	LD	5000	748

2) Subacute and subchronic toxicity:
   - a) More than 1/4th of an acute lethal dose daily, i.e. 100 mg/k (intraperitoneal) was required to yield 40% mortality of treated rats in 60 day exposures. 3204
     - (1) Duration of sublethal toxic action was very brief; complete recovery of intoxicated rats within a few hours of exposure to sublethal dosages was noted. 3204

3) Pharmacological, pharmacodynamical, physiological, etc.
   - a) Dipterex®, in vitro at 2×10^{-6} M, yielded 50% inhibition (I_{50} or ID_{50}) of rat brain acetylcholine esterase. 2120
   - b) The mechanisms and phenomena of toxic action presumably resemble those of the other "organophosphorus" toxicants and cholinesterase inhibitors, giving symptoms of cholinergic intoxication. (Consult the general treatment of Organic Phosphates in this work) 3204
   - c) To account for the rapid recovery of sublethally intoxicated animals a mechanism in mammalian biochemistry which brings about rapid reversal of Dipterex® induced cholinesterase inhibition in vivo has been suggested. 748
   - d) Atropine sulfate is reported to be antidotal. 3204
   - e) No traces of Dipterex® were found in milk of cows housed in treated barns; no flavor was imparted to milk. 3204
   - f) The metabolism of P^{32} labelled, radioactive Dipterex® in lactating cows of the Hereford breed: 2674
     - (1) After oral administration of Dipterex® at 25 mg/k the following were noted:
       - (a) Peak radioactivity in the blood achieved at 1-3 hours after treatment.
       - (b) In 2 hour sample 15.1 μg equivalents/cc, with 7.5% of the radioactivity attributable to unchanged Dipterex®.
       - (c) < 0.2% of the total dose radioactivity secreted in the milk by the 144th hour.
       - (d) In composite samples of milk (6-48th hrs.) < 10% of the radioactivity behaved (analytically) like unchanged Dipterex®. 23% of the radioactivity behaved (chromatographically) like inorganic phosphate and this was supported by *Musca* bio-assays.
     - (2) Dipterex® was rapidly metabolized by the cow and eliminated via the urine.
       - (a) Peak of elimination was achieved 2.5-5.5 hours after administration with 1.4 mg. equivalents per cc of urine.
       - (b) After 12 hours ca 66% of the dose was accounted for in urine.
       - (c) Chromatographically only 0.26% of the radioactivity excreted in this period was unchanged Dipterex®; 16.8% was dimethyl hydrogen phosphate or dimethyl hydrogen phosphite; ca 76% was composed of an unknown metabolite(s).
     - (3) It was indicated that the major metabolic pathway of Dipterex® in the cow is not by rupture of the P-C bond. No DDVP (q.v.) is to be detected in blood, milk or urine. Dipterex® is absorbed readily by the cow, as is attested by the small amount of radioactivity in the feces wherein only less than 3% of the dose may be accounted for.
     - (4) In grubs of *Hypoderma bovis*, taken from cows receiving oral Dipterex®, only low levels of radioactivity were dectable at various intervals after host treatment, the maximum being in grubs taken 6-24 hours after host treatment.

4) Phytotoxicity:
   - a) No data availabe to this compilation at time of preparation. Tests on at least some types of plants, which have indicated effectiveness against insect pests, would suggest that some plants tolerated, without harm, Dipterex® at insecticidal levels. 3204

5) Toxicity for insects:

5) Toxicity for insects:

a) Toxicology of Dipterex® (Bayer L 13/59) for insects (Musca domestica) with comparison of toxicity of Dipterex®, its homologues and derivatives: 150

Substance	LD$_{50}$ 24 Hrs, Topical, Musca domestica				I$_{50}$ (cockroach cholinesterase)	
	NAIDM (DDT-nonR)		Orlando-Beltsville (DDT-R)		Molar Concentration	Ratio To Tech Dipterex®
	(μg/fly)	Ratio To Tech Dipterex®	(μg/fly)	Ratio To Tech Dipterex®		
Dipterex® (tech)	0.395 ± 0.038	1.0	0.663 ± 0.067	1.0	6×10^{-5}	1.0
Dipterex® (purified)	0.315 ± 0.008	1.3	0.601 ± 0.038	1.1	4.2×10^{-5}	1.4
Ethyl homologue	> 5.0	—	— —	—	6×10^{-4}	0.1
Propyl homologue	> 5.0	—	— —	—	$> 10^{-3}$	< 0.01
Isopropyl homologue	> 5.0	—	— —	—	$> 10^{-3}$	< 0.01
Butyl	> 5.0	—	— —	—	$> 10^{-3}$	< 0.01
Dehydrochlorinated Derivatives						
Dimethyl-2,2-dichlorovinyl phosphate	0.013	30	0.037	17.9	9.4×10^{-7}	64.0
Ethyl homologue of DDVP	0.031	12.7	0.19	3.5	5×10^{-7}	120.0
Propyl	0.27	1.5	0.81	0.8	1.7×10^{-4}	35.2
Isopropyl	0.30	1.3	0.91	0.7	8×10^{-4}	7.5

(1) Addition of chlorinated terphenyls (e.g. Arachlor 5460) increased the residual effectiveness of Dipterex®; best effect at a ratio Dipterex® 1 to terphenyl 4 with 2-3 day old adult Musca domestica, adult and large nymph Periplaneta americana, adult Tribolium confusum, as test insects. 1588

Vs. Musca: Dipterex®-terphenyl at 100 mg/ft^2 gave 100% kills on 4-5 day residues, 97% on 10 day residues.

Vs. Musca: Dipterex® alone gave 100% kills for 2 hrs. only on treated surfaces; 12% kill on 4-5 day old; 16% kill on 10 day old residues.

Vs. Periplaneta: Dipterex®-terphenyl at 100 mg/ft^2 gave 100% kills on 10 day old residues; 31% kills on 30 day old residues.

Vs. Periplaneta: Dipterex® alone gave 100 % kills on 4-5 day old residues; 39% kills on 10 day residues; 0% kills on 30 day residues.

Vs. Tribolium (for which Dipterex® alone shows no residual effect): Dipterex®-terphenyl at 100 mg/ft^2 gave 20% kills on 4-5 day old residues; 32% kills on 10 day old and 2% kills on 30 day old residues.

b) Comparative effectiveness Dipterex® and other compounds for insects:

(1) As baits in control of flies: 1915

Insecticide		Laboratory Tests % Down Or Dead In			Field Evaluation; Control After 24 Hrs.
		30 min	1 hr	24 hrs	
Dipterex®	0.1%	54.5	56.5	100	Excellent control
Aldrin	1%	20	76	100	—
BHC	1%	43	76	100	—
Chlordane	1%	10	20	100	—
Chlorobenzilate	1%	0	0	60	—
DDT	1%	30	44	98	Unsatisfactory control
CS-708	1%	13	20	80	Fair control
Diazinon	1%	23	36	96	Excellent control
Dieldrin	1%	20	66	100	Unsatisfactory control
Heptachlor	1%	6	48	100	Unsatisfactory control
Lindane	1%	3	6	100	Unsatisfactory control
Lethane 384	1%	0	0	0	—
Malathion	1%	43	56	93	Excellent control
Metacide	1%	23	23	100	—
Methoxychlor	2%	23	20	93	Unsatisfactory control
NPD	1%	36	40	90	—
Parathion	1%	13	13	90	—
Strobane	1%	10	36	96	—
TEPP	.5%	53	56	100	—
Toxaphene	1%	40	56	100	Unsatisfactory control
Borax (saturated)		0	0	33	—
Boric acid	0.63%	3	3	50	—
Copper sulfate	2%	0	0	36	—
Formalin	2%	16	16	30	—
Cryolite	1%	0	0	0	—
Sodium fluoride	2.5%	0	0	66	—
Rotenone	0.3%	0	0	50	—

(2) Dipterex® and newer insecticides vs. lice of livestock: 2862

Insecticide	Concentration (%)	% Mortality 24, 48 Hrs.		Weeks Effective For Haematopinus	Infestation After 4 Weeks Bovicola
		As Spot Treatment On Cattle for Haematopinus eurystemus	As Dips for (On Goats) Bovicola caprae, B. limbatus		
Dipterex®	.25	100	—	1	—
"	.1	100	100	0	light
"	.05	—	100	—	light
"	.025	—	100	—	light
"	.01	—	100	—	light
"	.002	—	100	—	light
Bayer 21/199	.25	100	—	2	—
"	.2	100	—	2	—
"	.1	100	—	1	—
"	.05	100	—	1	—
"	.002	—	100	—	0
Bayer 21/200	.002	—	25	—	light
Pyrazinon	.25	100	—	3	—
EPN	.05	100	—	1	—
"	.01	100	—	1	—
"	.005	100	—	1	—
"	.002	25	100	0	0
Diazinon	.25	100	—	2	—
"	.1	100	—	2	—
"	.05	100	100	1	0
"	.025	—	100	—	0
"	.01	95	—	1	—
"	.005	25	100	1	light
"	.002	5	—	1	—
Chlorthion®	.25	100	—	1	—
"	.002	—	100	—	0
Tetrapropyl dithiopyrophosphate	.05	100	—	1	—
Malathion	.5	100	—	2	—
"	.25	—	100	—	0
"	.1	—	100	—	0
"	.05	100	100	1	0
"	.025	—	100	—	0
Parathion	0.05	100	—	3	—
"	.01	100	—	3	—
"	.005	25	—	0	—
DDT	0.5	100	—	4	0
"	.25	100	100	3	0
Toxaphene	.5	100	—	4	—
Strobane®	.5	100	—	1	—
"	.2	—	100	—	0
"	.1	—	100	—	0
Endrin	.05	—	100	—	0
Isodrin	.05	—	100	—	0
2-Pivalyl indanedione	1.0	100	—	3	—
"	.5	100	—	2	—
"	.25	100	—	2	—
"	.1	100	—	2	—
"	.05	100	—	2	—

c) Dipterex®, and other insecticides: Comparative toxicity for Heliothis zea and Heliothis virescens, 6th Instar larvae of 250-450 mg. weight; toxicants in topical application, as methylethyl ketone solutions, to the abdominal dorsum: 1124

Toxicant	LD_{50} (µg/g) For	
	Heliothis zea	Heliothis virescens
Dipterex® (Bayer L 13/59)	30	60
Toxaphene	2000	18,000
DDD	3000	17,000
DDT	3000	6,500
Endrin	17	180
Malathion	130	160
Bayer 17147	40	54
Shell OS-2046	4.8	4.8

d) Effectiveness of Dipterex® for insects; cage, field test evaluations: 3204

On Cotton plants: At 0.25 - 1.0 lb (active) per acre, promising vs. cotton aphids, spider mites, cotton leafworm, boll weevil. Ineffective vs. bollworm at 2 lbs per acre. Effectiveness reported vs. adult moths of pink bollworm.

Mosquito control: At 1 ppm gave 100% mortality of mosquito larvae.

Household, Warehouse insects: Tested with success at 1-2% concentrations vs. cockroaches (R and non-R strains), ants, crickets, silverfish.

e) Dipterex® in bait station use for control of *Musca domestica* in dairy barns, poultry houses, pig pens, feed lots (Florida, Kansas, Nebraska tests): 1764

(1) In 2% baits Dipterex® (and malathion) yielded excellent control where sufficient stations were used, and sanitation maintained at a level at least fair. Baits remained effective for 28 to 98 days.

f) May be used as a dry bait; as a liquid bait in sugar solution or in syrup, molasses, honey solutions; as a "varnish" painted on surfaces in corn syrup and blackstrap molasses; impregnated on cardboard disks to be placed in saucers with water.

Pharmacological, pharmacodynamic, physiological; insects:

a) Absorption and translocation of P^{32} labelled, radioactive Dipterex® in *Periplaneta americana*: 7

(1) Dipterex®, like its > toxic dehydrochlorination product DDVP (q.v.) is rapidly taken up by the cervical membrane following topical application.

(2) Distribution is widespread, the haemolymph and all tissues becoming radioactive.

(3) After 20 hours most of the radioactivity is in the gut. This is in sharp contrast to DDVP which is taken so rapidly by certain tissues that none is detectable in the haemolymph with concentration being high in the heart, and, after 22 hours, being highest in the fat body with but little present in the gut.

b) Synergistic action of piperonyl butoxide with Dipterex®: 2576

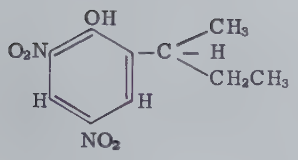
(1) In topical application to *Musca domestica* a synergistic effect has been noted between Dipterex® and piperonyl butoxide in terms of lethal effect.

(2) No *in vitro* effect of piperonyl butoxide has been noted on the anti-choline esterase activity of Dipterex® for bovine erythrocyte acetocholine esterase ("true" choline esterase). This is in contrast to the effects yielded by piperonyl butoxide on malathion (q.v.) action.

75

2,4-DINITRO-6-SEC.-BUTYLPHENOL

(4,6-Dinitro-2-sec.-butylphenol; 2-(1-Methyl-n-propyl)-4,6-dinitrophenol; 2-sec.-Butyl-4, 6-dinitrophenol; Dinitrobutylphenol; Dinoseb; DNBP; DNOSBP; DNSBP.)



Molecular weight: 240.212

GENERAL

[Refs.: 629, 2231, 353, 2120, 2832, 2815, 757]

An insecticide, acaricide and ovicide of the dinitrophenol group of insect and acarine toxicants. Originally described as an herbicide. The substance is highly toxic to insects both as an oral and contact insecticide. A very high phytotoxic potential and hazard largely confines use of Dinoseb as a dormant spray, or wash, on orchard trees. Poisonous and hazardous to animals. Consult in this work the general treatment titled Dinitrophenols, and also see DNOCHP, DNOC and dicyclohexylammonium dinitro-o-cyclohexyl phenate.

PHYSICAL, CHEMICAL

[2935, 2120, 2231, 2221, 1062, 1370]

The technical product: A dark, red-brown liquid; flammable; the pure product: A solid; m.p. 42°C [2120], 38°-39° [2231]; freezing point (technical product) ca 28°C; virtually insoluble in water (0.0734 g/100g) at 25°C; soluble in petroleum oils and many organic solvents for example, in ethanol (23.46 g/100g) petroleum oil (8.7 g/100 g); forms salts with alkalis (organic and inorganic bases) some of which, for example the ammonium salt, are water soluble. To be kept away from heat, open flames.

a) Formulations: In oil solution as an emulsion concentrate; as aqueous solutions of its water soluble salts, such as the triethanolamine salt, which in 36% water solution is sold as DN-289; as the technical product.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)		
Rat	or	LD_{100}	60	2,4 Dinitrophenol 100; DNOC 50; DNOCHP 180.	2935
Rat	or	LD_{50}	37	2,4-Dinitrophenol 35; DNOC 30; DNOCHP 65.	89, 2935
Rat	or	LD_{50}	40		129, 2231
Guinea Pig	or	LD (?)	25		129
Chicken	or	LD (?)	26		129
Guinea Pig	ct	LD_{100}	500	2,4-Dinitrophenol 700; DNOC 500; DNOCHP > 1000.	2231

2) Chronic and subacute toxicity; higher animals:

a) In 6 month feeding experiences with rabbits: 2935

(1) At 50, 100 ppm showed no observable effects.

(2) At 200 ppm showed loss in weight (3-8%;) some rise in urea nitrogen in serum.

(3) At 500 ppm, 4 animals of 10 dead (within 13 days) in state of marked emaciation; urea nitrogen level of serum very high; cloudy swelling of liver to some degree; degenerative kidney changes (slight).

b) In ducklings, opacity of the eye lens (cataract) may be induced by experimental exposure of birds to DNBP. 2935

c) Comparative toxicity for rats of DNBP and other dinitrophenol toxicants: 805, 2935

Substance	Tolerated Acute Dosage (mg/k)	LD_{100} (mg/k)	LD_{50} (Acute) (mg/k)	Tolerated In Diet (ppm)	Definite Damage At
2,4-Dinitrophenol	—	100	ca 35	200	500-1000 ppm
4,6-Dinitro-o-cresol (DNOC)	10	50	ca 30	100	200-500 ppm
2,4-Dinitro-6-sec.-butylphenol (DNBP)	5	60	ca 37	100	500 ppm
2,4-Dinitro-6-cyclohexylphenol (DNOCHP)	30	180	40; 80	500	1000 ppm
Dicyclohexylamine salt of DNOCHP	—	600	ca 400	500-1000	2000 ppm

3) Pharmacological, pharmacodynamical, physiological, etc.:
   a) For details and phenomena common to this group of toxicants consult, in this work, the general treatment, Dinitrophenols.
   b) DNBP is absorbable by ingestion, inhalation, and (in contrast to DNOCHP) may enter the body to a highly dangerous degree via the skin. May burn skin. 89, 353, 1221, 2231
   c) The mechanism of action (as in the whole group) is a pronounced increase in oxidative metabolism, with attendant elevated heat production. The action is primarily peripheral. 89, 2231, 1221, 353

4) Hazard:
   a) The hazard is comparable to that of DNOC, q.v., with DNBP absorbable via the skin even more readily than is the case for DNOC. 1569
      (1) Protective clothing, masks, regular examination are essential for formulations, steady handlers and applicators of DNBP. 1569

5) Phytotoxicity:
   a) DNBP, and the formulation of its triethanolamine salt called DN-289, are even higher in phytotoxic potential than DNOC. 353
   b) Originally introduced as a weed-killer and plant toxicant showing some selective action (for example, the triethanolamine salt of DNBP is less toxic for peas than are other compounds of the dinitro group.)
   c) As a 0.1% aqueous solution (triethanolamine DNBP) is safe as a dormant application to apple, plum and cherry trees. Presence of 0.5% oil in sprays induces bud injury ranging from light to moderate. 353
   d) Aqueous sprays of DNBP are toxic to peach trees, with severe damage to buds and terminal twigs. 1370
   e) A toxic soil contaminant more damaging than DNOC; 200 ppm inhibit plant growth, although 50 ppm are apparently stimulating to growth. Decomposed in the soil by micro-organisms. 353

6) Toxicity for insects and acarines:
   a) Comparative toxicity of DNBP and other compounds, for Bombyx mori (5th instar larva): 1743

Compound	Dosage Range, Intermediate Zone (mg/g)	Oral (Leaf Sandwich) LD_{50} (mg/g)
DNBP	0.008-0.011	0.009
DNOCHP	.004- .012	.007
2,4-Dinitro-6- :		
-cyclopentylphenol	.007- .012	.009
-n-octylphenol	.007- .014	.010
-n-heptylphenol	.003- .005	.004
-n-hexylphenol	.003- .006	.004
-n-pentylphenol	.007- .009	.008
-n-propylphenol	.011- .027	.018
-ethylphenol	.017- .057	.029
2,4-Dinitro-3-methyl-6-isopropylphenol	.028- .041	.033
DNOC	.03 - .072	.049
Rotenone	.002- .004	.003
Acid lead arsenate	.06 - .119	.09

   b) Toxicity of DNBP (as triethanolamine salt in form of DN-289) and other substances vs. the developmental stages of Tetranychus bimaculatus placed on Vicia faba treated with toxicants by the settling tower method of Ebeling and Pence. E = Emulsifiable Concentrate, W = Wettable Powder: 905

Compound	LC_{50} 48 Hrs. (g/100 cc)			
	Adult	Larva	Egg	Adult On Leaf Surface Opposite Treated Surface
DN-289 (Triethanolamine DNBP) E	0.0083	0.0072	0.038	0.24
DN-111 W	.082	.031	.28	1.44
Dinitrocapryl phenylcrotonate E	.036	.013	.24	1.43
Dinitrocapryl phenylcrotonate W	.066	.027	.53	3.6
Aramite E	.0038	.0072	.174	.041
Aramite W	.0041	.0082	.288	.055
DMC E	.044	.042	.082	.21
Neotran W	.62	.215	.30	5.0 +
Ovotran E	.45	.019	.076	5.0 +
Ovotran W	4.25	.028	.109	5.0 +
Parathion E	.0056	.013	.19	.021
Parathion W	.0045	.010	.37	.027
Malathion E	.0025	.0073	.32	.084
Malathion W	.0042	.0115	.84	.125
Diazinon W	.012	.028	.18	.115
Demeton E	.0022	.0028	.097	.003

7) Pharmacological, pharmacodynamical, physiological, etc.; insects:
   a) Also consult general treatment, Dinitrophenols, in this work.
   b) DNBP by injection at 10 μg/insect in Blattella germanica induced a very high initial rise in respiratory rate (O_2 consumption) followed by a rapid fall in respiratory rate. 1441

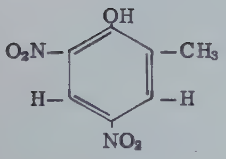
c) *In vitro* preparations of *Periplaneta americana* coxal muscle cytochrome c oxidase, as measured by O_2 uptake in the Warburg apparatus, were completely inhibited by 10^{-3} M concentrations of DNBP and stimulated by 10^{-5} M concentration. 2305

8) Field experiences in control of insects and acarines with DNBP:
   - a) Vs. *Psylla pyricola* (as 0.1% solution of DN-289): Highly effective at early bud stage. 1370
   - b) Vs. *Myzus*, *Hyalopterus*, *Anuraphis* eggs on apple, plum, cherry trees: 1 qt per gallon as DN-289 (0.07% DNBP) gave 97-100% control. 1370
   - c) Vs. *Lepidosaphes*, *Chionaspis*, *Aspidiotus perniciosus* eggs (as 1% DN-289 in dormant oil:) Gave 96-100% control. 1370
   - d) Vs. overwintering larvae of *Spilonota ocellaria* (as DNBP dormant spray): Gave 98-100% control. 1370
   - e) Vs. *Aceria sheldoni* on citrus trees, (as the dicyclohexylamine salt (DN-211) wettable powder:) Gave good control in preliminary field trials where the dicyclohexylamine of DNOCHP and 4,6-dinitro-2-caprylphenyl crotonate gave poor or no control. 1699

9) Screening tests:
   - a) For data showing the high effectiveness of DNBP vs. lice and their eggs, fleas, ticks, chiggers, in mosquito repellency, vs. cockroaches, and mosquito larvae consult Ref. 1801.

76

4,6-DINITRO-o-CRESOL (4,6-Dinitro-2-methylphenol; 2,4-Dinitro-6-methylphenol; Dinitrocresol; 3,5-Dinitro-orthocresol; DNOC; DNC; DN; 3,5-Dinitro-2-hydroxytoluene; Sinox; Antinnonin; etc., etc.)



Molecular weight: 198.13

GENERAL [Refs.: 353, 2231, 2815, 2832, 1059, 2120, 129, 89]

A potent insecticide, ovicide and acaricide, whose insecticidal properties have been appreciated since 1892. High phytotoxicity limits use largely to dormant sprays and washes for overwintering insects, acarines or their eggs, and as baits in control of such insects as grasshoppers, locusts, crickets. Highly toxic and hazardous to man and animals under certain circumstances. A member of the general group of toxicants referred to as dinitrophenols. Also consult, in this work, for data and phenomena common to the dinitrophenols, the general treatment under that designation. Used *per se*, or in the form of organic, inorganic, salts.

PHYSICAL, CHEMICAL [Refs.: 2120, 129, 2221, 353, 2231, 2935, 792, 3182, 89]

A yellow to yellowish, crystalline solid; crystal form prismatic; m.p. 85.8°C; b.p. 312°C; volatile with steam; v.p. 5.2×10^{-5} mm Hg at 25°C; soluble in water to 0.0128% w/w (128 ppm); soluble in many organic solvents, for example 2% w/w in kerosene, 20% w/w in aromatic oils, 40% w/w in xylene; in g/100 g solvent at 15°C: Acetone 100.6; benzene 37.5 carbon tetrachloride 2.4; chloroform 37.2; diethylether 9.12; ethanol 4.3; glacial acetic acid 23.45; methanol 7.3; petroleum ether 0.51; dormant spray oil (at 25°C) 5.98; readily soluble in alkaline aqueous media; odor none; a pseudoacid, it forms salts readily with metals, organic and inorganic bases, some of these salts, e.g. NH_4^+, Na^+, Ca^{++}, K^+, being water soluble; monobasic salts of DNOC are completely undissociated at pH 7, completely dissociated at pH 2; pK = 5.6; compounds formed with amines, phenols and hydrocarbons. Formulations: As the technical product, with 10% water to reduce explosive hazard; as salts in water solution, e.g. Elgetol (40% sodium dinitro-o-cresylate in water). Used in the form of dusts, as aqueous sprays of metallic or amine salts, as emulsions of DNOC, dissolved in oil as emulsion concentrate. 1.5-2.5% oil solutions and up to 40% water wettable powders are available, as are 20% salts in 14% oxidized oils.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   - a) The hazardous acute dose of DNOC for man is unknown, but is estimated as 2 grams, (ca 29 mg/k). DNOC is a cumulative poison, very slowly excreted in man. Persons who have shown symptoms, or whose blood level 8 hrs. after the last exposure is > 20 ppm, should be removed from further exposure for at least 6 weeks. 240, 237
   - b) Ingestion by human volunteers of a single 75 mg dose produced no toxic effects. 89
   - c) Applied as a 3% dust to open range for grasshopper control at 60 lbs per acre (= 1.86 lbs DNOC per acre) no effect was observed in calves pastured on the treated range for 3 weeks. 2385

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	sc	LD_{50}	24.2 (21.5-27.3)		2443
Rat	or	LD_{100}	50		2935
Rat	or	LD_{50}	30 (25-37)	Death in 1-2 hours.	2935
Rat	or	LD_{50}	ca 26		1951
Rat	sc	LD_{50}	24.6 (23.1-26.1)		2443
Rat	sc	LD_{50}	10		49
Guinea Pig	ct	LD_{100}	500	In alcohol solution.	2935
Dog	im	LD	5		1514
Dog	ip	LD	10		1514
Dog	iv	LD	15	Death in ca. 1 hour.	1514
Goat	or	LD_{50}	100		49
Goat	sc	LD_{50}	50		49
Pigeon	im	LD	5		
		(as sodium 4-6-dinitro-o-cresylate)			3045
Rat	or	LD_{50}	28		353
Rat	or	LD_{100}	40	Death in 1-8 hours.	49
Rat	sc	LD_{50}	ca 30	Death in 2-2 1/2 hours.	49
Fish	Medium	MLC	1.5-2 ppm	In distilled water.	1945
Fish	Medium	MLC	3 -4 ppm	In hard water (river).	1945

   - d) Comparative toxicity for the rat of DNOC and other dinitrophenols: 89, 2935, 805, 2935, 49, 353

Compound	Oral			Dermal Acute		
	Tolerated (Acute) (mg/k)	LD_{100} (mg/k)	LD_{50} (mg/k)	LD_{100} (Guinea Pig) (mg/k)	Tolerated In Diet (ppm)	Definite Damage At
DNOC	10	50	30	500	100	200-500 ppm
DNOC, Na salt	—	40	28	—	—	—
2,4-Dinitrophenol	—	100	ca 35	700	200	500-1000 ppm
DNBP	5	60	ca 37	500	100	500 ppm
DNOCHP	30	180	40; 80	> 1000	500	1000 ppm
DNOCHP, dicyclohexylamine salt.	—	600	ca 400	> 1000	500-1000	2000 ppm

2) Chronic and subacute toxicity; higher animals:
   - a) In feeding experiences with Rabbits, 6 month exposure to DNOC in the diet: 2935
     - (1) At 20, 50, 100 ppm gave no observable adverse effect.
     - (2) At 200 ppm showed 7%-9% loss of weight.
     - (3) At 500 ppm showed severe weight loss; elevated plasma urea nitrogen.
     - (4) At 1000 ppm: 5 of 10 subjects dead within 10 days; emaciated; high plasma urea nitrogen.
   - b) Rats have tolerated 100 ppm in diet without adverse effect. 353, 89
   - c) Goats have tolerated 2 g/day (50 mg/k/day) for 5 days without symptoms. 353
   - d) Dangerous cumulative toxicant for Man; concentrations of 5 ppm for several weeks may prove fatal. 240, 2221
   - e) For laboratory animals some report that there is little evidence of cumulative effect. 1439, 1796
   - f) Chronic toxicity stated to be 30 times less than that of sodium arsenite. 353
   - g) Man: Two volunteers received by mouth 75 mg/day for 7 days: In one subject lassitude, headache, malaise on 7th day; second subject no symptoms whatever. 89

3) Pharmacological, pharmacodynamical, physiological, etc.:
   - a) DNOC, in dangerous toxic amounts, may be absorbed by man and animals, via ingestion, inhalation or skin absorption. 89, 1569
   - b) As in the case of other dinitrophenols, DNOC increases the oxidative, and thus the heat productive, metabolism of the body by direct peripheral action. 89, 1737, 237, 1221, 49, 813
     - (1) Body temperature of laboratory animals was raised 3-5°C.
     - (2) In man, basal metabolism was increased without fever and, although the toxic and therapeutic doses are very close, DNOC has been used to reduce obesity.
   - c) Among lower organisms, DNOC inhibits the cleavage of sea urchin eggs, while increasing their respiratory rate; it inhibits synthesis of reserve materials by yeast. 1737
   - d) Inhibition of the synthetic processes of metabolism is reported due, almost certainly, to blockade of oxidative phosphorylation. 1737, 1221, 1738

e) Acceleration of metabolism by DNOC is explicable in two ways, both linked with phosphorylation reactions, though gaps in the hypothesis remain: 1737
   - (1) In vitro, the nitrophenols act on isolated cell particles (mitochondria?) containing the Krebs cycle enzymes, accelerating the respiration of these systems when they are deficient in inorganic orthophosphate or adenine nucleotide. 1737, 1738
   - (2) DNOC may interrupt phosphate transfer of both inorganic PO_4 and adenine nucleotide, thus making relatively more of these available to the respiratory mechanisms. 1737, 1738
   - (3) Rats, injected with lethal doses, revealed a sharp decrease of creatine phosphate, adenosine triphosphate, adenosine diphosphate, of all tissues and a sharp rise in inorganic phosphate and adenylic acid. 1737, 1738
   - (4) Studies with isolated rat diaphragms yielded results similar to (3), with progressive failure of stimulation response in poisoned muscle. Complete rigor, failure to respond to stimulus were correlated with an adenosine triphosphate level at the vanishing point.

f) Clinical aspects of DNOC poisoning in man:
   - (1) Signs, symptoms in man, closely resembled those in experimental animals and included: Nausea, gastric distress, restlessness, sensation of heat, skin flush, sweating, deep and rapid respiration, fever, cyanosis, collapse. The course of acute intoxication is rapid, with death or recovery within 24-48 hrs. the rule. 89
   - (2) Increase in metabolic rate proportional to dose (levels to 4 times the normal may be reached). Heat production may so outdistance heat loss as to induce fatal hyperthermia. 89
   - (3) The toxic action is aggravated by environmental heat. At 16°C, or below, external temperature increased oxidation and pyrexia do not occur. 237, 89
   - (4) Stimulation of metabolism is peripheral, independent of thyroxine, although final stages of intoxication imitate thyroid crisis. 237
   - (5) No antidote is known. In acute poisoning death may supervene in a few hours from heat stroke or cerebral oedema with dramatic change from apparent well-being to death within an hour or so. 237
   - (6) Signs of chronic intoxication may comprise: Fatigue, excessive sweating, thirst, loss of weight. Yellow staining of the sclerotics, conjunctivae, palms of hands, soles of feet, finger and toe nails, may indicate absorption but not necessarily poisoning. Among the early signs is often an exaggerated sense of well being (occurring on the 3rd or 4th day in experimental subjects). This euphoria indicates need for immediate break-off in DNOC exposure. 89, 237
   - (7) Those most likely to experience poisoning are: Contract sprayers, using DNOC on crops or as a selective weed-killer. Fatalities, in some number, have been recorded, almost all in spells of hot weather. No cases are reported in those using DNOC as a late winter or dormant spray. 237
   - (8) DNOC is cumulative in man and is excreted slowly (in contrast to laboratory animals in which it is more rapidly metabolized).

g) Experiences with human volunteers taking known dosages. 237, 89, 238
   - (1) 1 mg/k by mouth at 24 hr intervals gave gradual increase in blood concentration, reaching maximum 2-4 hours after ingestion.
   - (2) With predosage levels in blood at 15-20 μg/g, a further 75 mg dose brought sharp rise in blood concentration within 4 hrs. with lassitude, headache, malaise.
   - (3) Even without absorption of DNOC for 5 days, the blood concentration being ca. 10 μg/g, renewed administration brought a sharp rise in blood level which did not return to predose level for 24 hours. Exercise increased the blood concentration of DNOC.
   - (4) Skin application brought a rise in DNOC concentration of blood, but to a relatively slight scale. May produce burns on the exposed skin.
   - (5) Symptoms are recorded when the DNOC blood level reaches 40 μg/g.
   - (6) 6 weeks after final dosage, significant amounts still remained in blood stream.
   - (7) 24 hour excretion bears no fixed relation to DNOC blood level.
   - (8) 15-20 μg/g in blood, not less than 8 hours after last exposure to DNOC, is a danger sign, and exposure should be ended. Fatality recorded at blood level of 70 ppm.
   - (9) Treatment is symptomatic with administration of barbiturates, fluid and electrolyte replacement, cooling treatments. Sodium methyl thiouracil is reported to lower the basal metabolic rate of DNOC intoxicated subjects.

h) Pathology:
   - (1) In persons dead of DNOC poisoning, staining yellow of tissues, organs, fluids, has been noted. Lung congestion, oedema, and occasional petechial hemorrhages, are ordinarily present.

4) Phytotoxicity:
   - a) Highly phytotoxic; a potent herbicide. The damage to plants consisting of an acute necrosis without chronic injury suggests an effect on oxidative metabolism. 2676
   - b) More phytotoxic when applied in oil than in water.
   - c) Penetrates the leaf cuticle, or, as a gas, enters the stomata. May be used as a selective weed-killer on crops, e.g. wheat, which are not readily water wetted. In this way mustard plants (water-wettable) may be killed in stands of wheat. 1046
   - d) More phytotoxic as the undissociated pseudo-acid. 1046
   - e) McIntosh and Cortlandt varieties of apple are sensitive to oil sprays containing DNOC. 2120
   - f) At 3 lbs per acre, as an oil emulsion, has burned wheat foliage; at 5-10 lbs per acre (5 times the insecticidal dosage) has "scorched" broad-leaved plants. 360

g) Young shoots of coniferous trees are as susceptible as leaves of deciduous trees and shrubs. The older needles of conifers are more resistant. 1568

h) Restricted to dormant spraying in orchards. High temperatures as well as cool, humid, slow-drying conditions enhance phytotoxic hazard. 84

i) As the Na^+ salt (unactivated by presence of acid salts) the following dosages are tolerated by the plants named: Peas, flax 4 lbs/acre; sweet corn 6 lbs/acre; onions 8 lbs/acre; alfalfa 15 lbs/acre; barley > 30 lbs/acre. 3289

j) Decomposes in soil, leaving no toxic residue. 2676

5) Toxicity for insects and acarines:

a) Quantitative:

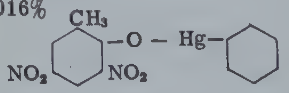
(1) As DNOC per se:

Insect	Route	Dose	Dosage	Remarks	
Aphis rumicis	Contact Spray	LC_{95}	ca 0.1 g/100 cc		3055
Aphis rumicis	Contact Spray	LC_{50}	0.05 g/100 cc		3055
Bombyx mori (5th instar)	or	LD_{50}	0.049 mg/g		1743
Agrotis orthogonia	Contact	L deposit $_{50}$	7.5 $\mu g/cm^2$		350
Choristoneura fumiferana	Contact	L deposit $_{50}$	4.0 $\mu g/cm^2$		350
Heliothis obsoleta (=armigera) larva	or	LD_{50}	$>$ 0.13 mg/g		1742
Heliothis ononis (larva)	Contact	L deposit $_{50}$	16 $\mu g/cm^2$		350
Paratetranychus citri	Contact	L deposit $_{50}$	1.8 $\mu g/cm^2$		1743
Locusta migratoria (young adult)	Topical	LD_{50} 96 hr	10.4 μg/locust	In tractor oil-cyclohexanone 9:1.	1585
Locusta migratoria (young adult)	Topical	LD_{50} 96 hr	9.9 μg/g	" "	1585
Locusta migratoria (young adult)	Topical	LD_{95} 96 hr	19.3±.897 μg/locust	" "	1585
Locusta migratoria (young adult)	Topical	LD_{95} 96 hr	18.3 μg/g	" "	1585
Selenia tetralunaria (eggs)	Contact Spray	LC_{50}	0.0147%		1175
Sitophilus granarius (adult)	Contact	ED_{50}	7.83×10^{-7}moles/$7cm^2$	Dry deposit from acetone sol. on filter paper.	2999
Sitophilus granarius (adult)	Contact	ED_{50}	1.24(1.19-1.3)moles/$7cm^2$	" "	2999
Sitophilus granarius (adult)	Contact	ED_{95}	2.68(2.52-2.85)moles/$7cm^2$	" "	2999
Sitophilus granarius (adult)	Contact	ED_{50}	1.04(.86-1.25)mg/cc	48 hrs. exp to films in P31 oil on paper.	2999
Tribolium castaneum (adult)	Contact Spray	LC_{50}	0.67% w/v	In ethylene glycol; 58-60°F post-treat. temperature.	2532
Tribolium castaneum (adult)	Contact Spray	LC_{50}	0.98% w/v	" 80.6°F "	2532

(2) As DNOC, sodium salt; sodium 4,6-dinitro-o-cresylate

Insect	Route	Dose	Dosage	Remarks	
Apis mellifera (adult)	or	LD_{50}	2.39 μg/bee @ 70°F	1/6 of LD_{50} ↑ O_2 uptake by 52%.	1209
Apis mellifera (adult)	or	LD_{50}	2.13 μg/bee @ 90°F	1/60 " " 28%.	1209
Apis mellifera (adult)	or	LD_{50}	13;23 μg/g		1209, 1717
Apis mellifera (adult)	or	LD	0.0028 cc	Of a spray with 1% active ingredient per 100 gallons.	1209
Periplaneta americana ♂	Topical	LD_0	0.015 mg/g	Av. wgt of insects=.9(.7-1.15)g*	2219
Periplaneta americana ♀	Topical	LD_0	0.18 mg/g	" " =1.3(1.0-1.9)g**	2219
Periplaneta americana ♂	Topical	LD_{50}	0.02 mg/g	*	2219
Periplaneta americana ♀	Topical	LD_{50}	.23 mg/g	**	2219
Periplaneta americana ♂	Topical	LD_{100}	0.03 mg/g	*	2219
Periplaneta americana ♀	Topical	LD_{100}	0.40 mg/g	**	2219
Periplaneta americana ♂	inj	LD_0	0.007 mg/g	*	2219
Periplaneta americana ♀	inj	LD_0	0.02 mg/g	**	2219
Periplaneta americana ♂	inj	LD_{50}	0.014 mg/g	*	2219
Periplaneta americana ♀	inj	LD_{50}	0.028 mg/g	**	2219
Periplaneta americana ♂	inj	LD_{100}	0.021 mg/g	*	2219
Periplaneta americana ♀	inj	LD_{100}	0.05 mg/g	**	2219
Selenia tetralunaria (egg)	Contact Spray	LC_{50}	0.016%		1175

(3) Toxicity of DNOC as DNOC phenyl mercury



Insect	Route	Dose	Dosage	Remarks	
Sitophilus granarius (adult)	Contact	ED_{50}	8.51×10^{-7}moles/$7cm^2$	as dry deposits from acetone sol. on filter paper.	2999

(4) DNOC vs. eggs of various aphids as MED_{95} (Minimum Effective Dosage for 95% kill) on tree bark: 525

Insect	MED_{95}	
	Spray Concentration (%)	Mg/100 cm² Of Bark Area
Aphis fabae	± .006	± 20
Capitophorus braggi	± .006	± 20
Rhophalosiphum prunifoliae	± .007	± 30
Aphis spiraecola	± .012	± 50

(4) DNOC vs. eggs of various aphids as MED$_{95}$ (Minimum Effective Dosage for 95% kill) on tree bark: 525

Insect	MED$_{95}$	
	Spray Concentration (%)	Mg/100 cm^2 Of Bark Area
Aphis pomi	± .012	± 50
Aphis abbreviata	± .012	± 50
Phyllaphis fagi	± .03	± 110
Myzocallis tiliae	± .03	± 110
Drepanosiphum platanoides	± .04	± 200

(5) Sodium 4,6-dinitro-o-cresylate: Toxicity for eggs of several insects measured as the amount (% in terms of DNOC) yielding 80% failure to hatch by dipping or dusting: 3185

Insect	Concentration (as DNOC) Yielding 80% Failure To Hatch (%)	
	By Dipping	By Dusting
Aphis pomi	0.1	0.06
Operophthera brumata	0.23	0.35
Ephestia kühniella	0.37	0.83

(6) Toxicity of DNOC in emulsified petroleum oil solutions vs. eggs of *Lygaeus kalmii* with toxicity of 2,4-dinitrophenol, similarly formulated for same, as comparison: 1743

Material	% Insecticide In Oil	% Mortality (Net) (% Mortality Controls = 40%)
Petroleum oil (2%)	0	0.0
Oil + DNOC (2%)	0.25	0.0
	0.5	36.7
	0.75	81.7
	1.0	90.0
	2.0	100
	3.0	100
Oil + 2,4-Dinitrophenol (2%)	0.5	13.7
	.75	23.8
	1.0	30.8
	2.0	50.0
	3.0	70.0

b) Structure and toxicity:

(1) Relation of length of side chain of 2,4-Dinitro-6-alkylphenols to toxicity for *Bombyx mori* (5th instar), treated by the leaf sandwich method: 1743

Compound	Dosage Range Intermediate Zone (mg/g)	Oral LD$_{50}$ (mg/g)
DNOC (2,4-dinitro-6-methylphenol)	0.03-0.072	0.049
2,4-Dinitro-6- :		
ethylphenol	.017-.057	.029
n-propyl phenol	.011-.027	.018
n-butyl phenol	.008-.011	.009
n-pentyl phenol	.007-.009	.008
n-hexyl phenol	.003-.006	.004
n-heptyl phenol	.003-.005	.004
n-octyl phenol	.007-.014	.010
cyclopentyl phenol	.007-.012	.009
cyclohexyl phenol	.004-.012	.007
2,4-Dinitro-3-methyl-6-isopropylphenol	.028-.041	.033
Acid Pb arsenate	.06 -.119	.09
Rotenone	.002-.004	.003

(2) For *Sitophilus granarius* adults the tetranitrophenol is non-toxic. 2999

c) Comparative toxicity for insects and acarines of DNOC and other substances:

(1) DNOC vs. *Periplaneta americana*, by contact (+ feeding through self-grooming) pure and in various concentrations in talc at 70°-80°F.: 1093

% Insecticide In Talc		% Kill In Hrs					
		3 hrs	6 hrs	12 hrs	24 hrs	48 hrs	72 hrs
DNOC	100% (no talc)	100	100	100	100	100	100
	50%	98	100	100	100	100	100
	25%	90	100	100	100	100	100
	10%	62	92	98	100	100	100
	5%	50	74	90	94	96	96
	3%	12	22	28	40	54	60
	1%	4	10	16	26	36	44

(1) DNOC vs. Periplaneta americana, by contact (+ feeding through self-grooming), pure and in various concentrations in talc at 70°-80°F.: 1093

% Insecticide In Talc		% Kill In Hrs 3 hrs	6 hrs	12 hrs	24 hrs	48 hrs	72 hrs
Sodium fluoride	100% (no talc	0	8	46	92	100	100
	50%	0	0	8	44	72	88
	25%	0	0	2	22	62	82
	10%	0	0	0	0	4	18
	5%	0	0	0	0	0	10
	3%	0	0	0	0	0	10
Pyrethrum	100% (no talc)	0	0	2	34	94	94
	50%	4	12	70	100	100	100
	25%	0	22	86	100	100	100
	10%	0	0	26	78	98	100
	5%	0	2	20	52	64	64
	3%	0	0	0	0	0	0
	1%	0	0	0	0	0	0

DNOC is more toxic for Periplaneta than pyrethrum or sodium fluoride; very toxic at concentrations in talc as low as 5%, with rapid decline in toxicity at lower concentrations although at 1%, 44% mortality is still achieved in 72 hrs.

(2) Approximate Lethal Deposit for adult Paratetranychus citri ♀♀ in μg/cm^2; DNOC and related substances: 1743

Compound	Approx. Lethal Deposit (μg/cm^2)
DNOC	1.8
DNOCHP	0.4
2,4-Dinitro-6-ethylphenol	1.2
2,4-Dinitrophenol	3.1
Dinitro-α-naphthol	> 3.4

(3) Comparative toxicities DNOC and other compounds for 3 insect types: Contact toxicity, measured as Lethal Deposit$_{50}$* μg/cm^2. * = Median Lethal Deposit. 350

Compound	Lethal Deposit$_{50}$ (μg/cm^2) For Choristoneura fumiferana	Heliothis ononis	Agrotis orthogonia
DNOC	4.0	16	7.5
DDT	0.3**	7	80
Lindane	1.9	23	5.5
Chlordane	140	negative	18
Nicotine	42	400	negative
Pyrethrins	0.05	4	8.2

**For complete control with DDT, 100 times the Lethal Deposit$_{50}$ dose is necessary.

(4) Comparative toxicity of DNOC and some other contact insecticides for Locusta migratoria migratorioides (young, virgin adults); tested by topical application; droplets of toxicants in mixture of tractor vaporising oil 9 parts to cyclohexanone 1 part as solvent: 1585

Insecticide		LD$_{50}$ 96 Hrs (μg/locust)	(μg/g)		LD$_{95}$ 96 Hrs (μg/locust)	(μg/g)
DNOC		10.4 ± .199	9.9		19.3 ± .897	18.3
Methyl parathion		0.94± .1	.89		2.3 ± .52	2.2
Lindane		3.89± .21	3.69		12.9 ± 2.09	12.2
Chlordane		20.4 ± 1.05	19.3		110.0 ± 30.9	104.0
Toxaphene	(LD$_{50}$ 5 day)	40.2 ± 2.88	38.1	(LD$_{95}$ 5 day)	123.0 ± 16.9	116.0
DDT	" "	140.0 ± 7.6	133.0	" "	258.0 ± 18.6	245.0

d) Hazard for beneficial insects:

(1) Highly toxic for bees. Hazard particularly great in blooming citrus groves where both pollen and nectar are contaminated. 906, 927 1209

6) Pharmacological, pharmacodynamical, physiological, etc.; insects:

a) DNOC is toxic by various routes: Contact, ingestion; it is toxic to insect eggs and to phytophagous acarines. [Refs.: 353, 2815, 2832, 315, 1175, 757, 2231, 1743, 2077]

(1) Contact effectiveness is claimed to be a function of affinity for insect cuticula. 353

(2) Highly toxic to all insects, even highly sclerotized forms (beetles) and hairy caterpillars (which are resistant to contact with rotenone and veratine dusts). Has a high mordant power. Toxic alike for eggs, larvae, pupae, adults. 2425, 2968

(3) Like a dye, DNOC is absorbed from oil or water by the insect cuticle, through, and along which, it migrates. 2968, 1717

(4) A direct action on the hypodermal cells, which it stains after passing through the cuticle, is claimed. 2968

(5) pH of the solution influences cuticular penetration. The undissociated molecule, which enters 792, 278
best from low pH solutions, gives the best toxic effect by contact. In 0.12% water solution at pH 2 279
DNOC gave 100% mortality of eggs of *Ephestia kühniella*, at pH 5 yielded no mortality. Salts, being alkaline, are less effective than DNOC *per se* as the undissociated pseudoacid. NH_4^+ salt shows the least diminution of insect toxicant power.

(6) Eggs (*Diataraxia oleracea*) are entered through the general chorionic surface and not via the micropyle 2730
or pore canals. DNOC attained the embryo proper within 1 hour. In these experiments DNOC as triethanolamine salt was used.

(7) Application to wings in *Locusta migratoria migratorioides* is ineffective (although in butterfly wings 2968
migration takes place to the insect body proper). Application to legs is most effective (most vulner- 1776
able point of surface entry) being 2 times as effective as application to head or abdomen. Applied as oil solution, the articular cuticula were the most readily penetrated.

b) Temperature modifies DNOC effectiveness in some insects, at least; susceptibility of *Lymantria* 1569, 2532
monacha larvae was enhanced at higher (physiological) environmental temperatures. For *Tribolium castaneum*, DNOC was 1.5 times as toxic at 60°F than at 80°F post-treatment holding temperatures.

c) DNOC manifested in insects (as in vertebrates) a swift metabolic acceleration, as measured by O_2 1441, 278
consumption. 1856, 1209
(1) *Blattella germanica*, 10μg/insect, by injection: Gave, in ca. 1 hr, O_2 consumption 3-4 times the 2041, 279
normal level. 2730

(2) *Melanoplus differentialis* (embryo) at 0.0001 M: Gave O_2 consumption 2.5 times the normal level but only for intact cells; maximum effect in acid media. Effect cancelled by CN, CO (involvement of cytochrome oxidase systems suggested).

(3) *Diataraxia oleracea* (egg) DNOC, triethanolamine salt: Respiration increased to maximum with return to normal all within 5 hrs, regardless of egg stage; 1, 2, 5 day eggs showed more marked respiration increase than 3, 4 day old eggs.

(4) *Apis mellifera*, DNOC, Na salt, oral: 1/6th LD_{50} dose increased O_2 consumption by 52%; 1/60th LD_{50} dose increased respiration by 28%.

(5) *Oryzaephilus*, *Tribolium*, *Blattella*: DNOC increased respiratory rate quickly in the early phase of intoxication (in *T.castaneum* 10 times the normal respiratory rate in 1 hr); rapid decline of respiratory rate in terminal phases.

d) DNOC dusted on *Lymantria monacha* larvae: Effects began within 1 minute: Restlessness, then convulsions, finally paralysis; death in 30-45 minutes. 1569

e) *Periplaneta americana*, *Blattella germanica* sprayed with DNOC: Showed exaggerated irritability to stimulus; tremors of the appendages before death. 2421

(1) Application to leg, *Periplaneta*: Spontaneous discharge; action potentials of crural nerve increasing in rate until leg contracted in 15 minutes, after which decline in frequency; voltage of the crural nerve discharge fading out in 45 minutes.

(2) By injection (80 μg), *Periplaneta*: Steady increase heartbeat rate to maximum in 10-50 minutes; beat of heart stopped in 1 hr. Transient stoppages of heart (diastolic) in phase of accelerated rhythm. Little stimulation of heart rate in decapitated insects suggests nervous mediation and a neurotoxic action.

7) DNOC in economic control of insects; field experiences largely:

a) A superb insecticide as baits, sprays, dusts, against Orthoptera, particularly on wastelands and breeding grounds where the high phytotoxic potential is no handicap. Has been used as aircraft-discharged dust on migrating locust swarms. Vs. *Melanoplus mexicanum* and *Nomadacris*, as a spray proved superior to BHC (10% γ-isomer). 353

b) Vs. *Locusta migratoria migratorioides*: Superior to BHC; as a dust, however, DNOC lacks the residual 1293
advantages and stomach toxicity of tech. chlordane. 359

c) Vs. grasshoppers in general: Effective at 1 lb per acre in sparse vegetation. 353

d) Vs. *Chlorochroa sayi*: Highly effective; superior to DDT, which kills slowly even with 10% dusts. Equally effective vs. *C. uhleri*. 353

e) Vs. *Oncopeltus fasciatus* (not susceptible to DDT): DNOC is highly effective. 356

f) Vs. *Blissus leucopterus*: 8% dusts formed an effective barrier and gave rapid kill. 160

g) Effective against aphids, mites, pear *Psylla* and black aphis of cherries.

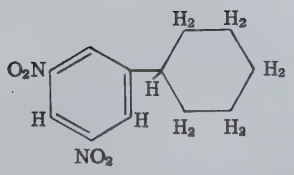
8) Screening test data:

a) For effectiveness in laboratory experiments vs. lice, fleas, ticks, flies, mosquitoes, cockroaches, trombiculid mites consult Ref. 1801.

77

2,4-DINITRO-6-CYCLOHEXYLPHENOL

(4,6-Dinitro-2-cyclohexylphenol; DNOCHP; Dinex®; Dry Mix No. 1 [Dow Chemical Co.]; 2-Cyclohexyl-4, 6-dinitrophenol.)



Molecular weight 266.248

GENERAL

(Also see Dicyclohexylammonium dinitro-o-cyclohexylphenate)
[Refs.: 353, 2231, 2120, 2296, 2815, 1059, 757, 129, 1742, 1743, 3182, 2077, 2293, 3055, 304, 592, 1663, 593, 1393, 2152, 99, 2175, 2903]

An established insecticide and acaricide; highly toxic by oral and contact routes to many insects, lethal to eggs of some insects. Highly phytotoxic, hence has use as an herbicide. Largely limited by the phytotoxic hazard to use in dormant washes, sprays and in baits. Belongs to that class of toxicants commonly referred to collectively as the dinitrophenols. Consult the general treatment of compounds of this class, and considerations common to all of them, in this work, in section titled Dinitrophenols.

PHYSICAL, CHEMICAL

[Refs.: 315, 2231, 353, 2120, 2221, 1742]

Highly poisonous, light-yellow, crystalline solid; m.p. 105°-106°C; v.p. low; soluble in water to 15 mg/l (128 ppm) at pH 6.5 and 25°C, at pH 1: 1.8 mg/l at 25°C; soluble in acetic acid and in many organic solvents, for example, solubility in g/100 g solvent (w/w): Acetone 40; benzene 109; carbon tetrachloride 22.6; ethanol 1.9; ethyl acetate 45.3; ethylene dichloride 64.1; kerosene 2; toluene 73.3; xylene 72.5; spray oils 2-3; dormant oil 16; forms salts with metals and organic bases, the cresylates of the alkali metals being water soluble; reacts with many amines, hydrocarbons, phenols; the metallic salts are potent insecticidal stomach poisons.

a) Formulations: 40% wettable powder (Dry Mix No. 1); as 1% dust on Frianite (a volcanic ash).

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) May be absorbed in toxic amounts by ingestion or inhalation; DNOCHP, in contrast to DNBP (2,4-dinitro-6-sec.-butylphenol) is not absorbed to an appreciable degree via the skin. 89, 2935

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	MLD	50-125	Given in olive oil.	1617
Mouse	sc	MLD	30-45	Given in olive oil.	1617
Rat	or	LD_{100}	180	Given in oil; death in 1-2 hrs.	2935
Guinea Pig	or	LD_{100}	125	Given in olive oil.	1617
Guinea Pig	sc	LD_{30}	20	Given in olive oil.	1617
Guinea Pig	ct	LD_{100}	> 1000		2935
Dog	sc	LD	8	Death in 30 minutes.	1514
Pigeon	im	LD_{50}	5		3045
Pigeon	iv	LD	6-7	Death in 8-10 minutes.	1514
Rat	or	LD_{50}	ca 65	Dicyclohexylamine salt; oral LD_{50} = 400 mg/k.	2231

(1) Comparative toxicity (for the rat) of 3 substituted dinitrophenols: 89, 2935

Compound	Tolerated Acute Dosage (mg/k)	Acute LD_{50} (mg/k)	Tolerated Conc. In Diet (ppm)
DNOCHP	30	80	500
DNOC	10	30	100
2,4-Dinitro-6-sec.-butylphenol (DNBP)	5	37	100

2) Chronic toxicity; higher animals: (Probably offers hazards similar to DNOC, q.v.) 2935

a) Rabbits: receiving DNOCHP in the diet, 6 months exposure: 2935

(1) At 200, 500 ppm showed 3-10% loss in weight (doubtful significance).

(2) At 1000 ppm showed 10%-15% loss in weight; slight decline in body fat; slight cloudy swelling of liver. Rats have tolerated 500 ppm administered in the diet.

b) Cataract of the eye, induced by chronic exposure of laboratory animals, and observed in man occasionally, by DNOC (dinitro-o-cresol) has not been observed with DNOCHP. Eye cataracts were not induced in ducklings with DNOCHP as has been done with DNBP. 185 2935

3) Pharmacological, pharmacodynamical, physiological, etc.:

a) The compounds of the dinitrophenol group stimulate and increase the oxidative metabolism and heat production of the body by direct peripheral action. Detailed consideration is given to them as a group in the general treatment, Dinitrophenols, in this work. 89 1221

4) Phytotoxicity:

a) The fact that DNOCHP is recommended for use as an herbicide suggests the high phytotoxic potential, shared to a greater or lesser degree by the whole dinitrophenol group of insecticides. The use of DNOCHP is thus largely limited to dormant sprays, washes, and baits. 2120 353

(1) Phytotoxicity is strongly influenced by environmental circumstances and formulations.

(2) Phase distribution of DNOCHP in water-oil emulsions is influenced by pH of the aqueous phase. % of DNOCHP remaining in the oil phase at equilibrium varies from $>$ 90% at pH 3.5-5.0 to $<$ 5% at pH 8-11. This phenomenon affects both the phytotoxicity and ovicidal properties of an emulsion. Optimum conditions (i.e. least phytotoxic hazard, highest ovicidal potential) are afforded by low (acid) pH. 315

b) Being somewhat less phytotoxic than DNOC and an effective acaricide, DNOCHP, with precautions, has been used as a summer spray. 439

(1) 0.02% suspensions (in absence of oil or lime sulfur) do not damage orchard foliage. 439
(2) 0.01% suspensions tend to "scorch" foliage of grape vines. 439
(3) 0.01% suspensions may "spot" and damage some greenhouse flowers. 439
(4) 0.25% in oil has proved harmless to citrus foliage. 315
(5) 0.5% in oil has done moderate damage to citrus foliage. 315
(6) 1.0% in oil has done severe damage to citrus foliage. 315
(7) Damage done to citrus by 0.5, 1.0% in oil is enhanced greatly under conditions of high temperature, low humidity. The margin of safety between insecticidal action and phytotoxicity is too narrow for oil solutions to be practical on plants in foliage. 315
(8) Dusts, prepared with an acid diluent (e.g. walnut shell meal) are not phytotoxic for citrus trees, peach or almond trees. 315
(9) Dusts, prepared with basic diluents, are injurious to tender shoots of citrus, peach and almond due to the formation of phytotoxic, water-soluble salts. 315

5) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Bombyx mori (4th instar)	or	LD_{50}	0.016 mg/g	By leaf sandwich method.	1381
Bombyx mori (5th instar)	or	LD_{50}	0.007 mg/g	By leaf sandwich method.	1743
Cirphis unipuncta (larva)	or	LD_{50}	0.015 mg/g		1742
Heliothis obsoleta (=armigera)(larva)	or	LD_{50}	0.087 mg/g		1742
Leptinotarsa decemlineata	or	LD_{50}	0.016 mg/g		1742, 1743
Melanoplus femur-rubrum	or	LD_{50}	0.065 mg/g		1742
Paratetranychus citri	Contact	L deposit$_{50}$	0.004 mg/cm^2		1743
Pieris (=Ascia) rapae (larva)	or	LD_{50}	0.073 mg/g		1742
Vanessa (=Cynthia) cardui (larva)	or	LD_{50}	0.02 mg/g		1381, 1743

Toxicity of metallic salts of DNOCHP

Calcium 2,4-dinitro-6-cyclohexylphenate				
Bombyx mori (4th instar)	or	LD_{50}	0.02 mg/g	1381
Cirphis unipuncta (larva)	or	LD_{50}	0.015 mg/g	1742
Heliothis obsoleta (=armigera) larva	or	LD_{50}	0.059 mg/g	1742
Pieris (=Ascia) rapae (larva)	or	LD_{50}	0.073 mg/g	1742
Vanessa (=Cynthia) cardui (larva)	or	LD_{50}	0.021 mg/g	1381
Copper 2,4-dinitro-6-cyclohexylphenate				
Heliothis obsoleta (=armigera)(larva)	or	LD_{50}	0.097 mg/g	1742
Lead 2,4-dinitro-6-cyclohexylphenate				
Heliothis obsoleta (=armigera)(larva)	or	LD_{50}	0.084 mg/g	1742
Magnesium 2,4-dinitro-6-cyclohexylphenate				
Heliothis obsoleta (=armigera)(larva)	or	LD_{50}	0.077 mg/g	1742

(1) Blattella germanica: Contact with a 50% DNOCHP dust in pyrophyllite at 0.81 mg/cm^2 deposit gave 75% kill in 24 hrs; 93% kill in 96 hrs; Average survival time ♂ = 1.3 hr; ♀ = 25.9 hr. 777

b) Comparative toxicity DNOCHP and other compounds:

(1) Toxicity of some 2,4-Dinitro-6-R-phenols for Bombyx mori; administered by the leaf sandwich method. Insects = 5th instar larvae. 1743

Compound	Bombyx mori		Leptinotarsa decemlineata		Cynthia cardui	
	Dosage Range Intermediate Zone (mg/g)	LD_{50} (mg/g)	Intermediate Zone (mg/g)	LD_{50} (mg/g)	Intermediate Zone (mg/g)	LD_{50} (mg/g)
DNOCHP	0.004-0.012	0.007	.007-.025	.016	.014-.030	.020
2,4-Dinitro-6-:						
-cyclopentylphenol	.007-.012	.009	.015-.030	.021	.039-.077	.050
-n-octylphenol	.007-.014	.010	—	—	—	—
-n-heptylphenol	.003-.005	.004	—	—	—	—
-n-hexylphenol	.003-.006	.004	—	—	—	—
-n-pentylphenol	.007-.009	.008	—	—	—	—
-n-butylphenol	.008-.011	.009	—	—	—	—
-n-propylphenol	.011-.027	.018	—	—	—	—
-ethylphenol	.017-.057	.029	—	—	—	—
2,4-Dinitro-3-methyl-6-iso-propylphenol	.028-.041	.033	—	—	—	—
3,5-Dinitro-o-cresol	.03 -.072	.049	—	—	—	—
Dinitro-α-naphthol	—	—	—	—	—	>.294
FOR COMPARISON:						
Acid lead arsenate	.06 -.119	.09	.055-.115	.08	.140-.190	.160
Rotenone	.002-.004	.003	.001-.004	.002	.021-.072	.030

(2) Survival times of Bombyx mori (5th instar) at various oral dosages of DNOCHP: 1743

Dosage Range (mg/g)	Mean Dosage (mg/g)	Mean Survival Time (hrs)	Toxicity Constant (k)
0.040-0.100	0.056	1.77	0.104
0.30 - .039	.035	1.63	.058
.020- .029	.025	2.76	.067
.010- .019	.014	4.87	.062
.004- .009	.007	14.20	.106

(3) Approximate Lethal Deposit for adult Paratetranychus citri (♀♀) DNOCHP and other compounds: 1743

Compound	Lethal Deposit ($\mu g/cm^2$)
DNOCHP	0.4
2,4-Dinitro-6-ethylphenol	1.2
3,5-Dinitro-o-cresol	1.8
2,4-Dinitrophenol	3.1
Dinitro-α-naphthol	>3.4

(4) Comparative effectiveness DNOCHP as a spray in 3 different mineral oil fractions for Chaoborus astictopus (ova) as measured by % mortality: 769

Conc. DNOCHP	In Kerosene		In Stove Oil		In Diesel Oil	
	cc/300cc H_2O	% Kill	cc/300cc H_2O	% Kill	cc/300cc H_2O	% Kill
0.5%	1.0	96.1	1.0	99.2	1.0	99.6
0.5%	.2	97.5	.2	99.7	.2	96.0
0.25%	1.0	94.1	1.0	100	1.0	100
0.25%	—	—	.2	100	—	—
0.1%	1.0	81.6	—	—	—	—
0.1%	0.2	78.0	—	—	—	—

(5) Toxicity, for Aspidiotus perniciosus, of DNOCHP-petroleum oil emulsions. Significance tested by χ^2 test. 1745

Treatment	% Oil + DNOCHP In Dilution	% DNOCHP In Oil	No. Insects	Total Dead	Mean % Mortality DNOCHP + Oil Mixture	Net Mortality* (%) Of DNOCHP
1% Petroleum Oil	1	0	1020	516	50.6	0
Petroleum Oil + DNOCHP	1	1	1020	768	75.3	50
	1	5	1020	906	88.8	77.4
	1	1	1020	996	97.6	95.2
	1	2	1020	1012	99.2	98.4
	1	3	1020	1012	100	100
CONTROL			1020	162	15.9	—
2% Petroleum Oil	2	0	900	770	85.6	0
Petroleum Oil + DNOCHP	2	1	900	859	95.4	68.4
	2	5	900	885	98.3	88.4
	2	1	900	898	99.8	98.4
	2	2	900	900	100	100
CONTROL			900	156	17.3	—

(a) Stock emulsion dilutions of 1% required 3% of DNOCHP in the oil phase to give 100% kill. Net mortalities of 98% were obtained with only 1/2 the concentration of DNOCHP required for 100% mortalities.

(6) Toxicity of DNOCHP for eggs of Lygaeus kalmii; DNOCHP solutions in oil made up in water emulsions. Significance tested by χ^2 test. 1745

Treatment	% DNOCHP In Oil Phase	No. Eggs	Dead		Total Dead	Mean % Kill DNOCHP+Oil Mixture	Net Mortality* DNOCHP
			Embryos	Hatched bugs			
1% emulsion							
Control 1% Pet.oil	0	250	21	5	26	10.4	0
	.1	250	29	5	34	13.6	3.6
	.5	300	80	19	99	33.0	25.2
	1.0	300	144	37	181	60.3	44.3
	2	300	126	120	246	82.0	79.9
	3	300	128	134	262	87.3	86.0
	5	250	110	132	242	97.0	96.6
	6.7	250	117	133	250	100	100
2% emulsion							
Control	0	500	204	9	213	42.6	0
	.1	500	273	34	307	61.4	32.8
	.5	500	342	32	374	74.8	55.5
	1.0	400	277	100	377	94.2	89.9
	2	400	269	120	389	97.2	94.8
	3	400	277	121	398	99.5	99.0
3% emulsion							
Control	0	500	280	22	302	60.4	0
	.1	500	311	56	367	73.4	32.4
	.5	500	338	116	454	90.8	77.5
	1.0	300	185	107	292	97.3	93.7
	2.0	300	184	115	299	99.7	99.3

* Net mortality % = x-y × 100 where x = % living in oil treated group; y = % living in oil + DNOCHP treated group.

(7) DNOCHP and its salts; toxicity for Tetranychus bimaculatus, residual effect, tested on Phaseolus coccineus in greenhouse experiences; total mites examined in each case from 500 + to 1100 +. Amount of substances used given in ounces per 100 gallon water + 1 lb DDT. 117

Days Between Spraying And Infesting	DNOCHP				NH$_4$-DNOCHP As DNOCHP				Monoethanolamine-DNOCHP As DNOCHP				DDT Alone	
	5 oz % Kill		2.5 oz % Kill		5 oz % Kill		2.5 oz % Kill		5 oz % Kill		2.5 oz % Kill		1 lb/100 gallons % Kill	
	7 da	14 da	7 da	14 da	7 da	14 da	7 da	14 da	7 da	14 da	7 da	14 da	7 da	14 da
1	99.8	100	89.8	72.6	99.0	92.6	81.7	26.7	87.7	89.6	58.3	21.2	2.9	3.2
3	92.9	94.8	59.0	70.4	78.0	70.1	34.3	25.2	79.6	69.8	20.7	11.6	4.0	5.7
7	82.9	80.0	38.3	32.4	52.2	33.1	8.8	16.3	11.9	40.0	10.2	10.3	3.9	14.0
10	86.4	99.6	23.4	—	37.9	—	13.9	—	26.0	—	6.1	—	4.3	—
14	60.2	61.0	10.7	—	19.8	—	14.5	—	14.5	—	8.3	—	6.5	—

(a) For comparison: Residual toxicity of Dinitro caprylphenyl crotonate (Arathane) for Tetranychus bimaculatus, tested on Phaseolus coccineus in greenhouse experiences as a 25% wettable powder 2 lbs per 100 gallons. Ca. 850 to 900 mites examined in each case: 117

Days Between Spraying And Infesting Of Plants	% Mortality After 7 days	% Mortality After 14 days	
1	94.3	90.2	Many eggs deposited before the death of the mites.
2	92.0	94.4	
3	94.4	84.8	
4	85.8	71.9	
5	91.2	77.3	
6	88.0	37.3	
7	77.3	24.0	
10	69.6	34.3	
14	87.1	52.1	
CONTROL	1.5	3.2	

(8) Field control experiences with DNOCHP as petroleum oil solutions + Na caseinate + water emulsions vs. Anuraphis rosae and Aspidiotus perniciosus: 881

Insect	% Control Achieved With Toxicant % By Weight In Dilute Spray			
	(.025-.6%)	(.05-1.2%)	(.1-2.4%)	(.15-3.6%)
Anuraphis rosae	95%	98%	99%	100%
Aspidiotus perniciosus	91%	99%	100%	—

6) Pharmacological, pharmacodynamical, physiological, etc.; insects: (Also consult the general treatment of Dinitrophenols in this work)

a) Mode of action:

(1) As in higher animals, carbohydrate breakdown of isolated tissues is increased; carbohydrate and fat metabolism of the intact insect are sharply increased. 1364

(2) In Apis mellifera: A 50% increase in O_2 consumption followed ingestion of 1/6th the LD_{50}. 1209

(3) Periplaneta americana, dusted with DNOCHP: Showed first a paralysis of the anterior followed by paralysis of the posterior portion of the body. 3182

(4) When DNOCHP was given by injection to Periplaneta americana there followed a gradual steady rise in rate of heartbeat until the heart finally stopped beating in about 1 hour. 2421

(5) At a concentration of 10^{-3} M, cytochrome oxidase from the coxal muscle of Periplaneta americana was stimulated, as measured by O_2 uptake in the Warburg apparatus; at concentration of 10^{-5}M an inhibitory effect on cytochrome oxidase was manifested. 2305

7) Hazard for beneficial insects:

a) DNOCHP is exceedingly toxic, particularly in citrus orchards in bloom, for the Honeybee, Apis mellifera. 906, 927

(1) Vacuum jar dusting tests of 10% DNOCHP vs. Apis mellifera showed kills of 2% at 4 hr, 4% at 6 hr, 10% at 12 hr, 12% at 24 hr, 13% at 48 hr, 17% at 96 hr at 400 mg dosage; 3, 5, 18, 20, 21, 23% kills respectively at 200 mg dosages, and 3, 3, 4, 6, 8, 8% at 100 mg dosages. 131

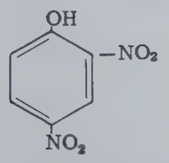
8) Field experiences in control of specific insect types with DNOCHP:

Vs. Chlorochroa sayi: Dusts proved very effective and superior to DDT. 353
Vs. Oncopeltus fasciatus: This insect, highly resistant to DDT, was highly susceptible to DNOCHP. 353
Vs. Blissus leucopterus: A very effective toxicant and barrier; superior to DDT. 160
Vs. Cicadellid, Jassid leafhoppers: Gave control, but DDT is supplanting DNOCHP. 3083
Vs. Aphids: Oil emulsions of DNOCHP as dormant sprays proved very effective ovicides. 1869
Vs. Lepidosaphes ulmi, Chionaspis furfura: Fairly effective as dormant spray in oil. 2226
Vs. Thrips tabaci: As a dust gave 90% control. 353
Vs. Epilachna varivestis: Ineffective. 353
Vs. Anthonomus pomorum, A. pyri: Ineffective. 786, 287
Vs. Acarina: Salts of DNOCHP proved highly effective to control summer generations. 2369
Vs. Tetranychus pacificus: Effective control at 0.03% concentrations. 2369
Vs. Paratetranychus ununguis: Erratic control; effectiveness decreased at low temperatures. 2705
Vs. Tetranychus bimaculatus: Addition of monoethanolamine-DNOCHP to TEPP sprays rendered these outstandingly ovicidal. 2705

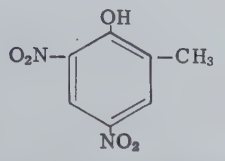
9) For screening test data on effectiveness of DNOCHP for lice, mosquito larvae, fleas, ticks, chiggers, flies, mosquito adults, consult Ref. 1801.

78

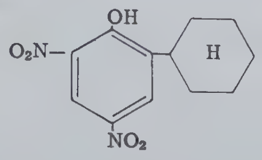
DINITROPHENOLS (GENERAL TREATMENT)
(Also consult the individual compounds in their particular treatments.)



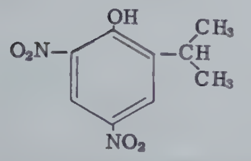
2,4-Dinitrophenol
(DNP)



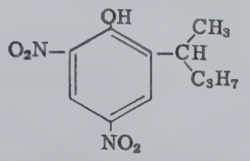
4,6-Dinitro-o-cresol
(DNOC)



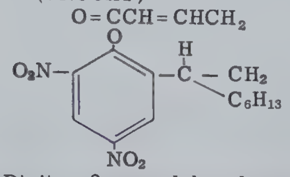
4,6-Dinitro-2-cyclohexylphenol
(DNOCHP)



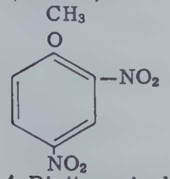
4,6-Dinitro-2-sec.-butylphenol
(DNSBP)



4,6-Dinitro-2-sec.-amylphenol



4,6-Dinitro-2-caprylphenyl crotonate



2,4-Dinitroanisole

GENERAL [Refs.: 353, 2231, 2815, 1059, 757, 1743, 1744, 2127, 1175, 217, 315, 336, 3182, 2077]

The substances whose formulae appear above (particularly DNOC, DNOCHP, DNOSBP and their metallic and amine salts) have found important use as insecticides, acaricides and ovicides. Collectively, they are referred to as the dinitrophenols. 2,4-Dinitroanisole has found use as a toxicant for eggs of lice in louse powders in military use (MYL powder) and 4,6-dinitro-2-caprylphenylcrotonate is an acaricide and fungicide. They have important common properties and effects which merit for them a general, comparative treatment as a class.

The potassium salt of DNOC has been used insecticidally since 1892. A high phytotoxic potential due to free phenolic groups (pseudoacids) is a major disadvantage of this class of insecticides. To overcome this disadvantage various metal and amine salts have been developed and used, for example, dicyclohexylammonium dinitro-o-cyclohexylphenate. These salts, while tending to be of lower toxicity for insects than the parent substances, yet remain exceedingly potent insecticides, ovicides and acaricides. For example, the LC_{50} of DNOC for the eggs of the moth *Selenia tetralunaria* = 0.0147% while the LC_{50} of DNOC, Na salt = 0.0167%. However, such structural alterations as the reduction of one nitro-group of DNOC to give 2-methyl-4-nitro-6-aminophenol yields a compound without ovicidal, contact or stomach toxicant properties for various insects.

The optimum conditions for use of DNOC, DNOCHP, with preservation of high ovicidal capacity and reduced phytotoxicity, are provided by strongly acidic mixtures, employed as dormant washes and sprays.

1) Chemical structure and toxicity for insects:
   a) Maximum activity among the phenols as insect toxicants is associated with presence of two nitro- groups. 3055
   b) In the alkyl dinitrophenols effectiveness as insect toxicants increases with length of the aliphatic side chain to a maximum at n-hexyl-or n-heptyl- with a decline in toxicity thereafter as chain length increases. 1742 1743,1745

Substance	LC_{50} (ca) g/100cc For *Aphis rumicis*	**	Substance	LD_{50}, mg/g, Oral For *Bombyx mori* (5th Instar)
p-Nitrophenol	0.25	(1.8) ←	2,4-Dinitro-6-methylphenol (DNOC)	0.049
o-Nitrophenol	1.0-2.5	(1.2) ←	2,4-Dinitro-6-ethylphenol	0.029
m-Nitrophenol	0.5-1.0		2,4-Dinitro-6-n-propylphenol	0.018
2,4-Dinitrophenol	0.1	→ (3.1)	2,4-Dinitro-6-n-butylphenol	0.009
Trinitrophenol	0.5-1.0		2,4-Dinitro-6-n-pentylphenol	0.008

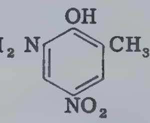
b) In the alkyl dinitrophenols effectiveness as insect toxicants increases with length of the aliphatic side chain to a maximum at n-hexyl- or n-heptyl- with a decline in toxicity thereafter as chain length increases. 1742 1743,1745

Substance	LC_{50} (ca) g/100cc For Aphis rumicis	**	Substance	LD_{50}, mg/g, Oral For Bombyx mori (5th Instar)
4,Nitro-6-methylphenol	0.25		2,4-Dinitro-6-n-hexylphenol	0.004
2-Nitro-5-methylphenol	1.0		2,4-Dinitro-6-n-heptylphenol	0.004
2-Nitro-3-methylphenol	0.5-1.0		2,4-Dinitro-6-n-octylphenol	0.010
2-Nitro-4-methylphenol	0.5-1.0		2,4-Dinitro-6-cyclopentylphenol	0.009
2,4-Dinitro-6-methylphenol (DNOC)	0.05	(0.4) ←	2,4-Dinitro-6-cyclohexylphenol	0.007
2,6-Dinitro-4-methylphenol	1.0		2,4-Dinitro-3-methyl-6-isopropylphenol	0.033
2,4,6-Trinitro-5-methylphenol	0.5	(>3.4) ←	2,4-Dinitro-α-naphthol	

** (Interpolated values) = Lethal Deposit$_{50}$ ($\mu g/cm^2$) for Paratetranychus citri adult ♀♀.

c) Toxicity for Aphis rumicis is linked to a nitro- group para to the hydroxyl-group; maximum toxic action is associated with 2,4-dinitrophenol alkylated at the ortho position. 3055

d) Modification of DNOC by reducing one nitro- group to yield 2-methyl-4-nitro-6-amino-phenol, brings loss of insect toxicity. 217 2127



2) Comparative toxicity of various dinitrophenols and their salts, by oral route, for various lepidopteran larvae and other insects: 1742,1743 1209,2219,1776

Insect	Oral LD_{50} (mg/g)							
	DNOC	DNOC, Na Salt	DNOCHP	DNOCHP, Ca Salt	DNOCHP, Mg Salt	DNOCHP, Pb Salt	DNOCHP, Cu Salt	4,6-Dinitro-2-cyclopentylphenol
Apis mellifera (adult)	—	0.002	—	—	—	—	—	—
Bombyx mori (5th I)	0.049	—	0.007	0.020	—	—	—	—
Cynthia (=Vanessa) cardui (5th I)	—	—	0.020	0.021	—	—	—	0.05
Cirphis unipuncta	—	—	0.015	0.015	—	—	—	—
Heliothis obsoleta (=armigera)	—	—	0.087	0.059	0.077	0.084	0.097	—
Leptinotarsa decemlineata (5th I)	—	—	0.016	—	—	—	—	0.021
Melanoplus femur-rubrum	—	—	0.056	>0.5	—	—	—	—
Pieris (=Ascia) rapae	—	—	0.073	0.073	—	—	—	—
	Topical$_{50}$ (mg/g)							
Locusta migratoria	0.010,0.015	—	—	—	—	—	—	—
Periplaneta americana	—	♂ 0.02 ♀ 0.23	—	—	—	—	—	—
	Injection LD_{50} (mg/g)							
Periplaneta americana	—	♂ 0.014 ♀ 0.028	—	—	—	—	—	—

a) Details of dinitrophenol toxicity as stomach poisons: 1742

Insect And Compound	LD_{50} (mg/g)	Lethal Zone			Sub-Lethal Zone		Intermediate Zone				
							Dead			Recovered	
		No.	Mean Survival Time (Hrs)	Dosage Range	No.	Dosage Range	No. No.	Mean Survival Time (Hrs.)	Dosage	No.	Dosage
Heliothis obsoleta											
DNOCHP	.087	6	3	(.149-.2)	26	(.009-.057)	22	4	.091(.06 -.125)	25	.082(.06 -.146)
" Ca salt	.059	20	3	(.109-.221)	27	(.013-.027)	24	5	.06 (.029-.105)	27	.058(.029-.107)
" Mg salt	.077	5	2	(.136-.188)	14	(.008-.04)	21	4	.082(.041-.133)	17	.073(.044-.134)
" Pb salt	.084	10	3	(.141-.232)	10	(.004-.053)	14	3	.088(.054-.128)	16	.08 (.054-.137)
" Cu salt	.097	5	3	(.157-.194)	23	(.011-.049)	19	4	.098(.051-.138)	14	.096(.053-.143)
2,4-Dinitro-6-phenylphenate, Ca	> .034 < .246	1	10	(.246-.246)	16	(.011-.033)	6	8	.06 (.034-.079)	36	.069(.034-.139)
DNOC, Pb salt	> .13				41	(.01 -.13)					
2,6-Dinitro-4-cyclohexylphenate, Ca	> .5				94	(.003-.5)					
Cirphis unipuncta											
DNOCHP, Ca salt	.015	26	4	(.022-.237)	12	(.001-.008)	22	9	.016(.009-.021)	21	.015(.009-.021)
Ascia rapae											
DNOCHP, Ca salt	.073	22	3	(.106-.336)	12	(.01 -.036)	17	6	.075(.042-.099)	19	.071(.043-.104)
Melanoplus femur-rubrum											
DNOCHP	.056	49	14	(.095-.913)	19	(.01 -.034)	13	20	.056(.035-.077)	12	.055(.036-.087)
DNOCHP, Ca salt	> .5				13	(.076-.5)	4	17	.664(.527-.81)	3	.694(.523-.93)

3) Dinitrophenols; toxicity for higher animals:

a) Toxicity for fish: 1945

Compound	MLC (ppm) Distilled Water	MLC (ppm) River Water (Hard)
o-Mononitrophenol	14-18	125-130
m-Mononitrophenol	9-10	20- 22
p-Mononitrophenol	4- 6	30- 33
β-Dinitrophenol	0.5-1.0	35- 38
DNOC	1.5-2.0	3- 4

b) Acute toxicity for mammals:

	Oral Toxicity (Rat)		Dermal Toxicity (Guinea Pig)	2935
Compound	LD_{50} (mg/k)	LD_{100} (mg/k)	LD_{100} (mg/k) Single Dose	1951
2,4-Dinitrophenol; DNP	35	100	700	
DNOC	30;26	50	500	
DNOCHP	65	180	> 1000	
DNOCHP, dicyclohexylamine	400;330	600	> 1000	
DNSBP	40	60	500	

c) Chronic and subacute toxicity of various dinitrophenols:

(1) Effects on the rabbit in 6 month feeding experiments; toxicants incorporated in the diet: 2935

Ppm in diet	DNP	DNOC	DNOCHP	DNOCHP, dicyclohexylamine	DNSBP
20	No effect	No effect	—	—	—
50	—	No effect	—	—	No effect
100	—	No effect	—	—	No effect
200	No effect	7-9% Wgt loss	3-10% Wgt loss	—	3-8% Wgt loss; Urea-N ↑
500	5-10% Wgt loss	Severe wgt loss; urea N↑	3-10% Wgt loss	Wgt loss, doubtful significance	4/10 dead in 13 days; emaciation, urea N↑; liver kidney effects.
1000	10-15% Wgt loss; emaciation; urea N↑; fat↓	5/10 Dead in 10 da; emaciation; urea N↑	10-15% Wgt.loss; body fat↓;liver cloudy, swelling	Wgt loss, doubtful significance	—
2000	4/10 dead in 21 da;urea N↑; kidney degeneration; liver cloudy swelling.			cloudy swelling of liver	—

4) Pharmacological, pharmacodynamical, physiological, biochemical, etc.; higher animals and insects:

a) Insects:

(1) Toxic by contact or ingestion. In contact toxicity, effectiveness is modified by the site of appli- 315,1175
cation. Although effective even for heavily sclerotized insects and insect eggs, the articular 1743,2077
cuticle seems, with DNOC, the most readily penetrated. Application of DNOC to legs of Locusta 2968,1717
migratoria was 2 times as effective as application to head or abdomen; application to wings pro- 2730,1776
duced little effect. pH of the solution influences toxicity, the undissociated molecule (in low pH 792
media) proving most effective. Shortly after surface application the cells of the hypodermis reveal deep staining. With DNOC, dose-mortality curves approximate well the dissociation curve. Likewise, in water emulsions of DNOC and DNOCHP oil solutions, the phase distribution of the toxicants in oil or water is, at equilibrium, strongly affected by pH. At low pH the balance of distribution is strongly in favor of the oil phase with correspondingly greater toxicity. Toxicity may be somewhat decreased, but is not lost, by salt-linkage with various metals and amines at the phenolic group.

(2) Although the mode of ultimate action in the cell remains unknown, the most characteristic effect 2305,2041
of these toxicants on insects is a great increase in O_2 uptake, with an enhancement of oxidative 1441, 278
metabolism. DNOC, for example, rapidly increased O_2 uptake to 10 times the normal level in 1 279,2730
hour in Tribolium castaneum; in Blattella 10 μg/insect resulted in 3-4-fold increase in 50-100 1209, 650
minutes of O_2 uptake over the normal. Eggs in all stages and embryos of Melanoplus manifest 151
the same effect provided the cells are intact. CN and CO cancel the effect, suggesting involvement of the cytochrome oxidase system which in vitro (Periplaneta coxal muscle cytochrome oxidase) is stimulated by DNSBP, DNOCHP at 10^{-5} M and inhibited at 10^{-3} M. DNOC and DNOCHP sodium salts, given orally to Apis mellifera, enhance the O_2 consumption. In the case of DNOC 1/6th and 1/60th the LD_{50} dose increased O_2 consumption respectively by 52% and 28%. DNOCHP was even more effective. 2,4-Dinitrophenol given to Galleria melonella at ca. 2/3rd the LD doubled the O_2 uptake.

(3) Symptoms, signs and effects of intoxication: DNOC, applied as a dust to Lymantria monacha 1569,3182
(larva), produced symptoms beginning in 1 minute: Restlessness then convulsions, followed by 1901,2421
paralysis, then death after 30-45 minutes. Dusts, applied to Periplaneta americana (DNOCHP), yielded paralysis spreading from front to rear of the body. DNOC, applied in oil to mouth parts, antennae, tarsi, frons of Locusta produced immediate signs of irritation. Spontaneous discharges from the crural nerve can be registered from the leg of Periplaneta treated with DNOC; frequency of discharge increases until flexion of the leg occurs in ca. 15 minutes, the voltage and frequency of discharge thereafter declining to extinction in 45 minutes after DNOC application. DNOCHP yields a similar response developing more slowly (90 minutes for flexion, 2-3 hours until extinction of the effect.) 80 μg DNOC or DNOCHP injected into Periplaneta americana gave a steady rise in heartbeat rate to a peak in 10-50 minutes; stoppage (final) in the heartbeat was preceded during the period of acceleration by diastolic halts of a transient nature. The effect could be produced but slightly, if at all, in headless insects. Little if any data or indications concerning histopathological effects of intoxication with dinitrophenols seem to be available for insects.

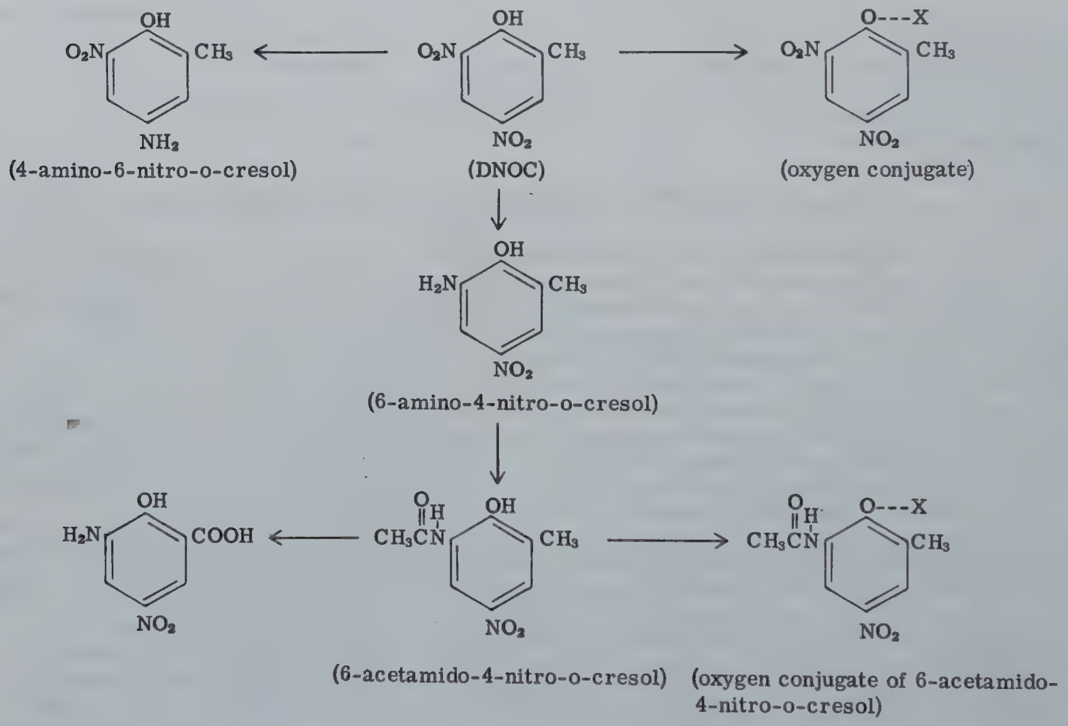
b) Higher animals; mammals:

(1) The insecticides of this group are highly toxic to man and other mammals. DNOC, for instance, is 353
highly dangerous to man being a strongly cumulative poison whose symptoms are aggravated by heat 89
and preceded by an exaggerated euphoria. Symptoms include: Sense of extreme warmth, excessive 1221
sweating, thirst, weakness, fatigue, collapse, and death, followed by almost immediate rigor.

(2) Absorption in mammals may be via the lungs (inhalation of vapors, mists, dusts), the skin (particularly 89
the case of DNOC, DNSBP, with DNOCHP being distinctly less hazardous by this route), the gastrointestinal tract.

(3) Differences in response of various vertebrate forms exist, for instance the rabbit seems more readily 1796
to detoxify and eliminate DNOC. When by any route the DNOC blood level in the rat reaches 100 μg/g a critical point is attained beyond which severe poisoning follows. In man 1 mg/k/day of DNOC may be cumulative because of slow removal; toxic symptoms appear at a blood level of 20 μg/g. Tissues of humans dead of DNOC have revealed tissue concentrations no greater than 5 μg/g, the average being ca 1 μg/g.

(4) The biochemical fate of DNOC has been studied in some detail in the rabbit. At dosages of 20-30 mg/k less than 20% appears as urinary metabolites, 5% being unaltered DNOC and 1% an oxygen-conjugate. Principal metabolites are 6-amino-4-nitro-o-cresol derivatives (to 11-12% of the DNOC dosage,) 6-acetamido-4-nitro-o-cresol derivatives (to 1.0-1.5% of DNOC dosage,) oxygen-conjugates of 6-acetamido-4-nitro-o-cresol (to 10% of dosage,) with traces of 3-amino-5-nitrosalicylic acid and 4-amino-6-nitro-o-cresol. Detoxification occurs chiefly by reduction of the 6-nitro group to give 6-acetamido-4-nitro-o-cresol (0.05 as toxic as DNOC). The following schema has been proposed:


OH
O₂N
CH₃
NH₂
(4-amino-6-nitro-o-cresol)
OH
O₂N
CH₃
NO₂
(DNOC)
O---X
O₂N
CH₃
NO₂
(oxygen conjugate)
OH
H₂N
CH₃
NO₂
(6-amino-4-nitro-o-cresol)
OH
H₂N
COOH
NO₂
O H
CH₃CN
OH
CH₃
NO₂
(6-acetamido-4-nitro-o-cresol)
O H
CH₃CN
O---X
CH₃
NO₂
(oxygen conjugate of 6-acetamido-4-nitro-o-cresol)

(5) Mode of action.

I. The action of certain nitrophenols, e.g. DNOC and 2,4-dinitrophenol (DNP) in marked elevation 1737,1738
of metabolic rate of animals is supported by extensive experimental and clinical evidence. 1735,1221
2036,1835

(a) That the action is on a protean level in the metabolism of cells is suggested by the fact that 217,1265
cleavage (mitosis) is inhibited in sea urchin eggs at the same time that respiration is accelerated. 657,3042
2311, 813

(b) In growing yeast cultures, synthesis of cell reserve materials is blocked.

II. The experimental evidence which follows supports a postulate that nitrophenol action is fundamentally a blockade of oxidative phosphorylation, in which oxidation and phosphorylation are uncoupled.

(a) DNP inhibits reversibly in low concentration the uptake of inorganic orthophosphate associated with glutamate-oxidation by cell-free kidney extracts. The action is confirmed in similar preparations using adenosine-5-phosphate, Mg^{++}, F^{-}, yeast hexokinase and fructose. Sharp phosphate uptake block occurred at DNP concentrations of 10^{-5} -2 x 10^{-4} M, with respiration unaffected or slightly enhanced.

(b) 2,4-dinitro-6-aminophenol and 2,4-dinitro-1-naphthol-7-sulfonic acid had similar but lesser activity compared with DNP in the uncoupling of oxidation from phosphorylation. Metabolites of DNP (viz. 2-amino-4-nitrophenol, 2-nitro-4-aminophenol) lacked influence either on phosphate uptake or respiration.

(c) Inorganic orthophosphate and adenosine-5-phosphate are both essential for the oxidation of glutamate at the maximum rate in the forementioned system. Omission of either depresses glutamate oxidation rate by 70%.

(d) DNP, in low concentration, enhances glutamate oxidation in orthophosphate deficient systems to almost the same degree as orthophosphate *per se*.

(e) DNP and other nitrated phenols, which can uncouple oxidation from phosphorylation, will, to an extent, substitute for adenosine-5-phosphate and increase the respiration of systems deficient in inorganic orthophosphate and adenosine-5-phosphate. DNP influence is lessened in absence of F^-.

(f) Washed kidney microsomes (mitochondria?) oxidise acetate if catalytic amounts of tricarboxylic acid cycle substrate are available to "prime" the reaction. Low concentrations of DNP inhibit acetate oxidation in such systems.

III. Using washed microsomes (mitochondria?) of liver, kidney, origin (rat, rabbit) it has been demonstrated that ca 1×10^{-4} M DNP blocks pyruvate oxidation. The block is lifted by Coenzyme I, ATP and l-malate. These phenomena have supported a view that transphosphorylation between a labile phosphate ester and ATP is blocked at three points (from pyridine nucleotide to flavoprotein to the cytochrome cycle) by DNP. Metabolic acceleration by DNOC may be explained in two ways, both having to do with phosphorylation reactions.

(a) Since nitrophenols act *in vitro* on isolated mitochondria containing Krebs cycle enzymes, by accelerating the respiration of such systems when deficient in inorganic orthophosphate or adenine nucleotide, then:

(b) DNOC probably interrupts phosphate transfer of both inorganic orthophosphate and adenine nucleotide, thus making relatively more of these available to the respiratory mechanism.

(c) Rats, which received lethal doses of dinitrophenols, showed *sharp decline* in creatine phosphate, ATP and ADP of all tissues and *increase* of inorganic phosphate and adenylic acid. Isolated rat diaphragm responded similarly to DNOC. In the presence of dinitrophenols, the muscle progressively failed to respond to stimuli. When the ATP level reached the vanishing point complete rigor and failure to respond occurred.

(d) Certain suggestive indications from insect studies with DNOC give hints that similar mechanisms are involved in insect intoxication.

(e) Respiratory and glycolytic acceleration of the poisoned cells is a sequel of availability of orthophosphate and adenylic acid phosphate acceptors which ordinarily keep the glycolytic metabolism within normal physiological bounds. Since, in the uncoupling of phosphorylation and oxidation, there is no depressing action by DNP on respiration, aerobic oxidation instead of forming energy-rich phosphate is turned to heat generation and dissipation.

(6) *Dinitrophenol poisoning; clinical and other aspects.* 237,89,1221

(a) All the dinitrophenols of insecticidal interest enhance oxidative metabolism and increase the body's heat production by direct action on cell metabolism (peripheral action).

(b) Onset of metabolic action (with DNP) is immediate after intravenous injection and in man 3-5 mg/k, orally, within the hour increases, by 20-30%, the metabolic rate. The effect endures 24 hours. Daily repetition of the dose maintains a 50% increase in metabolic rate.

(c) Response to DNP, DNOC, etc., differs fundamentally from that elicited by thyroxine: DNP enhances selectively the oxidation of fat (fall in respiratory quotient). Increased cardiac output is not apparent. Respiratory change is sharply increased. DNP does not relieve the symptoms of thyroid deficiency, nor speed the developmental processes, like thyroxine.

(d) Metabolic rate increase is proportional to dose. However, fatal hyperthermia at a certain level, when the capacity for heat loss is overtaxed, supervenes. 10 mg/k in man may raise the rectal temperature by 3°F.

(e) In man, the dangerous dose of DNOC is estimated to be 2 g (29 mg/k). The toxicant is cumulative, slowly excreted, and the appearance of the early signs of intoxication imposes an immediate termination of any possible further exposure. *The early signs of DNOC poisoning include*: Sweating, thirst, fatigue (often in handlers of DNOC attributed to hot weather, long hours, etc.) and a *prime sign*, namely: *An exaggerated euphoria and feeling of being more fit than usual*. The appearance of this sign in spraymen, handlers, formulators, etc., dictates immediate halt to further DNOC exposure. Yellow staining of sclerotics, while indicating absorption, does not necessarily indicate poisoning.

(f) *Late manifestations of DNOC poisoning*: These result from the stimulation of the general metabolism, and are aggravated by heat. Although the stimulation is peripheral and independent of thyroxine the final stages of intoxication resemble thyroid crisis. Those most likely to be affected are persons occupationally exposed to DNOC and other dinitrophenols, namely: Contract sprayers, formulators and applicators of DNOC as a selective weed-killer. Most of the fatalities among such exposed workers have occurred in periods of unusually hot weather, when the hyperthermic action of the poison is exacerbated by environmental high temperature. Few, if any, cases are reported from operators applying DNOC as a winter spray. *See under 4,6-dinitro-o-cresol detailed data derived from human volunteers who have taken known doses of DNOC.*

(g) Symptoms appear when the blood level of DNOC reaches 40 µg/g.
(h) Manifestations of acute poisoning with dinitrophenols include: Nausea, gastric distress, restlessness, sensations of heat, flushed skin, rapid respiration, fever, cyanosis, death followed quickly by rigor mortis. The course of acute poisoning is rapid and fatal. There is no antidote known. Treatment is supportive: Cold baths, spongings, oxygen administration, restoration and maintenance of the electrolyte balance disturbed by excessive sweats.
(i) In experimental animals cataract (corneal opacity) has been induced by chronic exposure. In man DNP administration has shown the eye to be susceptible; cataract developed in 1% of patients under DNP therapy.
(j) There is no specific, or typically characteristic, tissue pathology.

79

DIPHENYLENE OXIDE

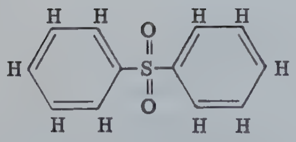
1) Toxicity for insects:

Datana perspicua (larva)	or	LD_{50}	0.96 (0.53-1.48) mg/g	1381
Mosquitoes (culicine) (larva)		LC_{50}+	5 ppm (16 hr exposure)	1001

a) Applied to wounds of farm animals, protects against infestation by *Cochliomyia americana*. Phenothiazine-resistant *Cochliomyia americana* remains susceptible to diphenylene oxide. 2441 1830

80

DIPHENYL SULFONE (DPS; Phenyl sulfone; Sulfobenzide.)



Molecular weight: 218.27

GENERAL [Refs.: 900, 898, 1808, 896, 901, 2120, 2231, 353]

Unsubstituted diphenyl sulfone, described as an acaricide with virtually no insecticidal activity and particularly effective against the eggs and adults of *Metatetranychus ulmi* (= *Paratetranychus pilosus*), is related to p-chlorophenyl sulfone (Sulfenone®) q.v., and more remotely to azobenzene and other diphenyl compounds with various bridging groups (-N=N-, $-\overset{NO}{\underset{}{N}}-$, -NH-NH-, $-CO-O-CH_2-$, -CH=CH-CO-etc.) which have shown more or less acaricidal and acarine ovicidal action. Although giving very good results against summer stages of the fruit tree red spider mite, diphenyl sulfone is inactive against the winter eggs. As a compound, it illustrates the observation that acaricidal activity is associated with molecules having two benzene nuclei bridged by certain groups of which $-SO_2-$ is one of the more effective. The toxicity of such molecules is influenced both by alterations in the bridging group and in the benzene nuclei, for instance chlorine, in para- position, is associated with maximum acaricidal activity. Compounds with $-\overset{\displaystyle O}{\underset{\displaystyle O}{\overset{\|}{\underset{\|}{S}}}}-$ as the bridge between the benzene nuclei show a higher acaricidal activity in case of the mono-para-chloro than in case of the di-para-chloro substituent. Interestingly enough diphenyl sulfine, which is unsubstituted in the benzene nuclei, is almost equal in toxicity to Metatetranychus ulmi summer eggs and adults as is p-chlorophenyl sulfone.

PHYSICAL, CHEMICAL

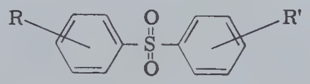
In the pure state: A colorless crystalline solid; as the technical (commercial) product: An off-white, grayish solid; m.p. (pure) 128-129°C, (technical) 115°C; b.p. (pure) 378-379°C; virtually insoluble in cold water, slightly soluble in boiling water; soluble in hot alcohol, in benzene, and various polar and aromatic solvents; stable at ordinary temperatures toward acids, alkalis, oxidants and reductants; compatible with commonly employed spray materials. Formulated as wettable powders (doubtfully effective); miscible concentrates in solvents with surface active agents (effective but costly); suspensions of finely ground diphenyl sulfone in white oil (fairly effective, not costly).

TOXICOLOGICAL

1) Toxicity for higher animals:
No data available. On analogy with p-chlorophenyl sulfone toxicity may be presumed to be low. The acute LD_{50} (oral) of p-chlorophenyl sulfone for mice is 3650 mg/k. Fed at 1000 ppm in the diet of rats, p-chlorophenyl sulfone showed no adverse effect or indication of toxicity. 3319

2) Phytotoxicity:
a) The phytotoxic hazard is apparently low. There is evidence of a temporary adverse action on some apple tree varieties when diphenyl sulfone is applied with lime-sulfur at 0.5% by volume. 896, 898
b) No phytotoxicity developed on the following varieties of apple tree grown in Great Britain: Cox, Worcester, Lane's Prince Albert, Sunset, Lord Lambourne, Ellison's Orange, Late Cox, Tydeman's Early Worcester, James Grieve, Arthur Turner, Miller Seedling, Beauty of Bath, Grenadier. 896, 1807

3) Toxicity for acarines and insects:
a) Has proven effective in the field with excellent control of *Metatetranychus ulmi* summer eggs and adults when used in a solvent + emulsifier + spreader formulation in one application. Wettable powders have proved much less successful. 896
b) Ineffective toward *Paratetranychus citri*. Inferior to azobenzene, q.v., as an ovicide for *Tetranychus telarius*. Little activity as an insecticide for *Plutella maculipennis*. 896,2228 2587
c) Other reports indicate that applied to apple trees at 0.1% + powdered derris (sufficient to give a rotenone concentration of 0.004%), diphenyl sulfone gave excellent control of *Metatetranychus ulmi* without leaf or fruit damage. Alone, at 0.1% in early and late applications, diphenyl sulfone gave some, but inadequate, control. Use of DPS alone as early or late applications was deemed a definite failure in the field.
d) Comparative toxicity for *Metatetranychus ulmi* of DPS and other diphenyl sulfone derivatives: 2231, 900



R	R′		Concentration (%)	% Mortality *M. ulmi*	
				Summer Eggs	Adults
H	H	(DPS)	0.1	98.1	69.3
H	H	(DPS)	.025	83.3	63.1
4-Cl	H	(Sulfenone®)	.1	96.0	80.9
4-Cl	H		.025	75.9	65.6
4-Cl	4-Cl		.1	0	—
4-Cl	4-Cl		.025	—	54.1
4-Cl	4-CH_3		.1	30.7	50.3
2,4,Di-NO_2	4-CH_3		.1	0	30.8
2-OH, 5-CH_3	2-OH, 5-CH_3		.1	0	8.6
3-Cl, 4-OH	3-Cl, 4-OH		.1	3.9	45.0
2-OH, 5-Cl	2-OH, 5-Cl		.1	4.4	50.8
2-CH_3, 4-OH	2-CH_3, 4-OH		.1	0	24.8
3-CH_3, 4-OH	3-CH_3, 4-OH		.1	0	7.5
3-NH_2	3-NH_2		.1	0	10.8

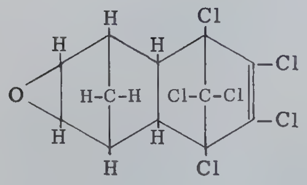
e) DPS: Toxicity in field experiences vs. *Metatetranychus ulmi* at dosages of 400 gallons per acre applied as sprays on orchard trees: Formulations: 20% wettable powder; 10% dispersible acetone solution; 35% in oil-water emulsion: 896

Treatment	% Mortality, Eggs (Days After Spraying)		% Mortality, Mites (Days After Spraying)	
	8 days	15 days	8 days	15 days
0.2% by weight in acetone	49.2	61.4	97.1	52.9
0.2% by weight as oil-H_2O emulsion	56.0	91.6	91.4	94.7
1.0% by volume in Shell summer oil	55.0	81.8	67.3	85.6
0.1% by weight as wettable powder	no control; mite "population" increased after spraying.			

(1) Optimum control obtained with application at a time when the majority of winter eggs have hatched, but before there is an appreciable hatch of summer eggs. Sprayed trees remained free of large mite "populations" throughout the summer. The action is selective against mites, the predators being left unharmed.
(2) For screening test data see Ref. 1801.

81

ENDRIN (1, 2, 3, 4, 10, 10-Hexachloro-6, 7-epoxy-1, 4, 4a, 5, 6, 7, 8, 8a-octahydro-1, 4-endo, endo-5, 8-dimethanonaphthalene; Hexachlorooctahydro-endo, endo-dimethanonaphthalene.)



Molecular weight: 380.926

GENERAL

[Refs.: 2812, 1756, 1757, 1988, 353, 2231, 2640, 2639]

Endrin is one of a group of insect toxicants referred to collectively as cyclodiene insecticides, highly chlorinated cyclic hydrocarbons characterised by an endomethylene-bridge structure. Besides endrin, the group includes aldrin, chlordane, dieldrin, heptachlor, isodrin and toxaphene, q.v. Synthesis of all (save toxaphene) is by the Diels-Alder diene reaction. Endrin is identical to the principal constituent of dieldrin except that the latter is the endo-exo-isomer whereas endrin is the endo-endo-isomer. Endrin is a highly active toxicant for insects as a general poison, killing both by contact, and by stomach action. Like the other members of its group, endrin has found extensive field use, and has demonstrated striking potency against Orthoptera, flies (and other household insects), cotton plant insects, etc.

PHYSICAL, CHEMICAL

Pure: A white crystalline solid; technical: A light-tan, powdery, crystalline solid; mild "chemical" odor; m.p.: At more than 200°C melts and decomposes; density (bulk) 55-60 lbs/ft^2, 14.6 lbs/gallon at 68°F; v.p. 2×10^{-7} at 77°F, 25°C; settling point: Rearranges when heated to more than 392°F; solubility (for details see table below): Insoluble in water; sparingly soluble in methanol; low solubility in aliphatic hydrocarbons (ca 0.1 lb/gallon); soluble in xylene to ca. 3.3 lbs/gallon; emulsibility potential good; excellent stability in storage (although less stable than dieldrin) and stabilized in formulations by small amounts of hexamethylene tetramine; not corrosive; not flammable; compatible with most chemically neutral, or alkaline, agricultural chemicals; tends to rearrange to a less insecticidally active substance in combination with acids, some metallic salts and catalytically active dust carriers although deactivation of diluents and carriers to form stable mixtures with endrin is practicable, for example by, use of hexamethylene tetramine.

Formulations: Emulsible (emulsifiable) concentrates in aromatic solvents; dust concentrate 25%; 1 and 1.5% dusts; as granules (solutions of endrin sprayed on granular, sorptive carriers).

a) Solubility of endrin in various solvents at 77°F, 25°C:

Solvent	In Saturated Solution (% By Wgt)	g/100 cc	g in 100 cc
Acetone	28	31	26
Aerosol 4555	29	39	31
Amyl acetate	24	28	23
Aromac 10A	20	26	22
Benzene	37	51	37
Bronco Hi Sol 4	32	45	35
n-Butanol	7	6	6
Carbon tetrachloride	24	51	38
Cyclohexanone	44	74	51
Diesel oil	11	10	10
Ethanol	4	3	3
Ethylene dichloride	41	87	53
Exosol	32	43	34
Fuel oil	11	10	10
Isopropanol	4	3	3
Kerosene	6	5	5
Methanol	3	2	2
Methyl cellosolve	10	11	10
Methyl ethyl ketone	33	40	31
Mineral spirits	9	8	7

a) Solubility of endrin in various solvents at 77°F, 25°C:

Solvent	In Saturated Solution (% By Wgt)	g/100 cc	g in 100 cc
Sovacide 544-C	32	40	35
Toluene	46	74	51
Trichloroethylene	41	100	63
Turpentine	19	21	18
Velsicol AR 50	35	53	40
Xylene	39	55	41
Water	< 0.1 ppm	—	—

b) Vapor pressure of endrin = ca. 1/30th that of aldrin; approximately equal in vapor pressure to dieldrin and DDT. Residual activity duration: Longer than aldrin; almost equal to DDT.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) May be absorbed by ingestion, inhalation, or via the unbroken skin. The dermal route offers the most serious occupational hazard.

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat (6 mo old) ♀	or	MLD	<5	Dilute solution 0.1-1.0% w/v in peanut oil.	3120
Rat (6 mo old) ♀	or	LD$_{50}$	7.3	" "	3120
Rat (26-31 day old) ♂	or	MLD	5-7	" "	3120
Rat (26-31 day old) ♂	or	LD$_{50}$	28.8 (16.2-51.2)	" "	3120
Rat (26-31 day old) ♀	or	MLD	7-10	" "	3120
Rat (26-31 day old) ♀	or	LD$_{50}$	16.8 (13.0-21.7)	" "	3120
Rat (6 mo old) ♂	or	MLD	24-36	" "	3120
Rat (6 mo old) ♂	or	LD$_{50}$	43.4 (39.3-47.9)	" "	3120
Rabbit ♀	or	MLD	5-7	" "	3120
Rabbit ♀	or	LD$_{50}$(estimate)	7-10	" "	3120
Rabbit ♀	ct	(?)LD$_{100}$(8/8)	250-3600	Dry, 24 hrs exp. of intact skin; 100 mesh pwdr.	3120
Rabbit ♀	ct	(?) (2/3)	160	" "	3120
Rabbit ♀	ct	(?) (1/3)	125	" "	3120
Rabbit ♀	ct	(?)caMLD (1/3)	94	" "	3120
Rabbit ♀	ct	(?)caLD$_0$ (0/3)	60	" "	3120
Guinea Pig ♀	or	MLD	10-16	Dilute solution 0.1-1.0 w/v in peanut oil.	3120
Guinea Pig ♀	or	LD$_{50}$(estimate)	16	" "	3120
Guinea Pig ♂	or	MLD	24-36	" "	3120
Guinea Pig ♂	or	LD$_{50}$(estimate)	36	" "	3120
Cat ♂ ♀	or	MLD	<5	" "	3120
Monkey ♂ ♀	or	MLD	1-3	" "	3120
Monkey ♂ ♀	or	LD$_{50}$(estimate)	3	" "	3120
Chicken (7 days old)	or	LD$_{50}$	3.5	In acetone; by capsule; older birds more resistant.	2824

2) Subacute and subchronic toxicity; higher animals (multiple exposures):

a) Oral administration, as 0.025 or 0.1 (w/v) % solution in peanut oil, on each of 50 days for 67-72 days. 3120

Animal	Age At Start	Daily Dosage		
		1 mg/k	2 mg/k (No. Dead/No. Treated)	5 mg/k
Rabbit ♀	8-10 weeks	4/5	—	—
Rat ♀	29 days	0/3	1/2	—
Rat ♀	6 months	0/3	1/3	—
Rat ♂	29 days	0/3	0/3	—
Rat ♂	6 months	—	0/3	3/3

b) Intermittent cutaneous exposure; ♀ Rabbits, exposed 2 hrs/day for 5 days/week over several weeks. Endrin as dry, pure powder (100 mesh screen) under rubber sleeve on unbroken skin: 3120

Doses Applied	Daily		Skin	Number Dead/Number Treated
	Grams	g/k		
19-25	0.15	0.067-0.091	Intact	3/3
40-70	0.075	0.020-0.042	Intact	1/3
25-45	0.075	0.027-0.044	Abraded	1/4

c) Intermittent exposure to endrin vapor in air; exposure time 7 hrs/day, 5 days/week at 5.44 μg/liter (0.36 ppm): 3120

Animal	Exposure Duration (Hrs)	Number Dead/Number Exposed
Cat	910	0/1
Guinea Pig	910	0/2
Hamster	707-910	0/2
Rat	910	0/3
Rabbit*	826	2/4
Mouse**	749	1/3

* 3 survived 12 periods of exposure each 7 hours long.

** 6 survived 18, 18, 42, 58, 64, 64 exposure periods each 7 hours long.

d) Sub-chronic toxicity of endrin to chickens 1 week old at beginning of exposure: 2825

Concentration (ppm)	Mean Kill (%)	Mean Wgt Gain (Survivors At 7 Wks) (g) ♂	Mean Wgt Gain (Survivors At 7 Wks) (g) ♀	Mean Food Consumed g/Chicken 1 Wk	Mean Food Consumed g/Chicken 2 Wk	Efficiency Of Conversion To 3 Weeks Of Age
12	95	no survivors	461.5	88.9	102.5	4.41
6	15	714.3	626.9	103.3	194.0	2.2
3	0	802.8	685.8	120.9	195.1	1.96
1.5	0	845.6	702.1	128.6	194.1	2.02
0	0	842.9	703.6	133.4	191.6	2.01
LSD (5%)		54.8	37.8	36.7	37.3	1.17
LSD (1%)		73.0	50.2	50.5	51.4	1.61

3) Chronic toxicity; long term feeding experiences; endrin given in the diet: 3120,3123

a) Rats fed 2 years on diets containing endrin:

	Amount in Diet (ppm)		Number Dead/Number Exposed ♂ 80 Wks	♂ 106 Wks	♀ 80 Wks	♀ 106 Wks
Level Of Significant Kill ♂	100	Level of Significant Kill ♀	18/20*	18/20	18/20*	19/20
	50		13/20***	16/20	19/20*	20/20
	25		5/20	9/20	12/20**	15/20
	5		♀5/20	13/20	7/20	12/20
	1		5/20	9/19	4/20	9/20
	0		7/20	12/20	5/20	13/20

* P = <0.01

** P = 0.05-0.01

*** P = but slightly >0.05

(1) Average length of survival ♂♂♀♀ at 100 and 50 ppm and ♀♀ at 25 ppm significantly less than controls. At 1 and 5 ppm; survival time ♂♂♀♀ not significantly less than controls.

	At 100 ppm	50 ppm	25 ppm	5 ppm	1 ppm	
(2) Average survival (wks) ♀♀	11.6	8.9	64.7	81.4	93.3	92.5 (controls.)
Average survival (wks) ♂♂	11.7	53.3	86.1	90.1	90.5	80.6 (controls.)

(3) Gain in weight of ♀♀ at 1, 5, 25 ppm = to or > than controls.
Gain in weight of ♂♂ at 1 or 50 ppm = to or > than controls.
Gain in weight of ♂♂ at 25 ppm significantly reduced and at 5 ppm retarded during first 20 weeks only.

(4) ♂♂ for 2 years on 25 or 5 ppm showed liver to body weight ratios significantly greater than controls. Not true for ♂♂ fed at 1 ppm or ♀♀ at 1 or 5 ppm.

(5) Rats fed at 50 or 100 ppm developed hypersensitivity to external stimuli, occasionally convulsions, signs not observed at 25 ppm or less.

(6) Rats dead during test at 100, 50, 25 ppm showed diffuse brain, liver, kidney, adrenal degeneration. Survivors of 100 and 50 ppm feeding showed hepatic degenerative change only. Animals at 1 and 5 ppm gave normal visceral findings.

(7) 50, 25, 5, 1 ppm fed over 106 wk to ♂♂: Endrin caused no significant increase of mortality over controls; at 100 ppm only 5% survived beyond 2 weeks.

(8) ♀♀ are more susceptible than ♂♂; 100, 50, 25 ppm gave significant increase in mortality and reduced length of survival. After 80th week at 25 ppm no increase in mortality of ♀♀ (over controls) was apparent.

(9) Increase in relative weight of kidneys appeared among ♀♀ fed at 5 ppm, but not at 1 ppm; increase not observed among ♂♂ at 25, 5, 1 ppm.

b) Experiences with dogs, receiving endrin in the diet; toxicant introduced in diet 6 days per week: 3120,3123

Amount In Diet (ppm)	Amount In Diet mg/k/day	Number; Sex	Duration Of Experience (mos.)	Result
50	2.5-4.0	♂ 1, ♀ 1	18-20 (days)	Death, 2
25	1.21-2.2	♀ 2	18-30 (days)	Death, 2
5 for 2.9 mo 20 for remainder	0.25-0.36 0.97-1.27	♀ 1	4.7	Death

Amount In Diet (ppm)		Amount In Diet mg/k/day	Number; Sex	Duration Of Experience (mos.)	Result
10		0.49-0.81	♂ 1, ♀ 1	24-44 (days)	Death 2
8		0.29-0.62	♂ 1, ♀ 1	5.7	Dead 1; survived 1
2	for 2.9 mo	0.09-0.17	♂ 1, ♀ 1	9.9	Dead 1; survived 1
8	for remainder	0.31-0.65			
5		0.2 -0.27	♂ 1	47 (days)	Death
4		0.15-0.21	♂ 1, ♀ 2	5.7	Survived
3		0.12-0.25	♂ 2, ♀ 2	18.7	Survived
1		0.045-0.12	♂ 2, ♀ 2	16.4-18.7	Survived
0		0	♂ 1, ♀ 1	18.7	Survived (3 others survived 5.7 mos)

(1) Dogs, receiving 10-50 ppm, all died as did more than 1/2 of those on 5-8 ppm. All survived at levels less than 5 ppm, viz. 3 and 1 ppm.

(2) All dogs on 10 ppm or more showed extensive weight loss; at 8 ppm gain of weight early, but eventual loss; at 4 ppm growth not normal; at 3, 1 ppm growth as in controls.

(3) Dogs, receiving toxic concentrations, became lethargic, regurgitated food, showed salivation and finally complete anorexia with emaciation, respiratory distress, leading to central nervous symptoms (hypersensitivity to stimuli, tremors, twitchings, extensive convulsion. Dogs, on 4, 3, 1 ppm gave no intoxication symptoms.

(4) At 8 ppm for ca 6 months produced hepatic, renal and brain enlargement; reduction in deposit of peritoneal, omental fat. After 19 months at 3 ppm yielded significant heart and kidney enlargement. Ratio of liver, brain, spleen, fat weights to total weight at 3, 1 ppm were not significantly different from controls.

(5) No relative or absolute change in peripheral blood cell types, or numbers, in dogs on 3, 1 ppm for 18.7 months.

(6) Animals dead of intoxication during experiment showed diffuse, degenerative lesions (brain, heart, liver, kidneys) plus pulmonary hyperaemia and oedema. Renal damage was severe: Diffuse degeneration and necrosis of convoluted tubules. Liver: Diffuse degeneration, fatty vacuolation, sometimes necrosis of hepatic cells; changes more marked in central lobular zone. Dogs surviving diets with 8 ppm yielded normal visceral findings.

(7) Endrin in tissues of dogs surviving 6 months of 4, 8 ppm: fat, liver = 1 ppm; kidneys (at 8 ppm) = 0.5 ppm; at 4 ppm = 0; brain at 4, 8 ppm = 0.

c) Further experiences with rats receiving endrin in the diet: 2367

Endrin In Diet (ppm)	Sex	Mortality At 4th Weeks' End (No.Dead/No. Exposed)	(%)	P*	Mortality At End 10th And 16th Weeks (No.Dead/No. Exposed)	(%)	P*
100	♂	5/5	100	.004	5/5	100	.006
50	♂	4/5	80	.02	5/5	100	.006
25	♂	2/5	40	.22	3/5	60	.068
5	♂	2/5	40	.22	3/5	60	.068
1	♂	0/5	0	—	3/5	60	.068
0	♂	0/5	0	—	0/5	0	—
100	♀	5/5	100	.004	5/5	100	.004
50	♀	2/5	40	.22	3/5	60	.046
25	♀	3/5	60	.046	4/5	80	.02
5	♀	0/5	0	—	0/5	0	
1	♀	0/5	0	—	0/5	0	
0	♀	0/5	0	—	0/5	0	

* Less than .05 considered significant. (Chi square test, with Yates' correction for small numbers.)

(1) ♂♂ more sensitive to endrin than ♀♀.

(2) Weight loss proportional to dosage at 100, 50, 25 ppm levels (reduced food intake of endrin fed rats not entirely responsible).

4) Comparative toxicity, for higher animals, of endrin and its chemical relatives: 3120,3128, 50 1647,1951,2231

a) In single acute oral dose, endrin is ca. 3 times as toxic (for the rat) as aldrin, and 15 times as toxic as DDT. 3120

b) In prolonged feeding, rats can consume ca 3 times as much aldrin, 12 times as much DDT, without increase in relative weight of specific organs (liver, kidney). 3120

c) Dogs are ca. 10 times as susceptible to endrin intoxication as to DDT intoxication, judged by growth rate and relative weight of specific organs. 3120

3120,3128

Animal	Oral/LD_{50} (mg/k) In Peanut Oil Solution Endrin	Aldrin	Dieldrin	Isodrin	DDT
Rat (25-31 days)	♀ 16.8 ♂ 28.8	♀ 45.9	♀ 38.3	♀ 16.4 ♂ 27.8	—
Rat (6 months)	♀ 7.3 ♂ 43.3	—	—	♀ 11.7 ♂ 42.1	—

c) Dogs are ca. 10 times as susceptible to endrin intoxication as to DDT intoxication, judged by growth rate and relative weight of specific organs. 3120

3120,3128

Animal		ct MLD (mg/k) Applied As Dry Powder; Single 24 Hr. Exposure				
		Endrin	Aldrin	Dieldrin	Isodrin	DDT
Rabbit ♀		60-94	600-1250	250-360	< 94	>2500
		ct MLD Daily Dose (mg/k); Repeated Application (2 hrs/day, 5 days/week for 10 weeks)				
Rabbit ♀	dry pwdr.	< 30	35-123	40-163		213-489
Rabbit ♀	in veg. oil		10-26	19-50		109-257
Rabbit ♀	in Ultrasene		< 4.8	< 5.3		> 46

Animal	Oral LD_{50} (mg/k)							
	Endrin	Aldrin	Dieldrin	Isodrin	Chlordane	Heptachlor	Toxaphene	Strobane
Rat	10-12	67	87	12-17	457-590 (tech) 700 (α)	90	69	200
Chicken (7 days)	3.0	25.5	43.0	2.7	—	—	—	—
	Ct LD_{50} Single Dose; Dry (mg/k)							
Rabbit		< 150	< 150	—	< 780	2000	> 4000	—
	Ct LD_{50} Repeated Daily Exposure (mg/k)							
Rabbit		< 5	< 5		20-40	< 20	40	

5) Effects of endrin on wildlife; (game birds). Quail, Pheasant: 780, 781

a) Toxicity to adult quail and pheasants (10 birds at each level of feeding, ca 100 controls of each species):

Level			Consumed (mg/k)		Mortality	Survival
(%)	(ppm)		(daily)	(total)	(%)	(Days)
			Quail			
0.5	5000		62.9	92.5	100	2
.25	2500		7.2	13.9	100	2
.125	1250		2.6	9.2	100	4
.0625	625		1.8	4.5	100	3
.01	100		0.9	4.4	100	5
.005	50		.6	2.8	100	5
.001	10		.7	16.7	100	26
.0005	5		.5	11.3	100	22
.0002	2		.2	6.4	100	36
CONTROL					4.1	154
			Pheasant			
.01	100	♂	.6	5.0	100	9
		♀	1.1	25.3	100	23
CONTROL					3.6	100

b) Toxicity to young quail and pheasant (1 day old at start); continuous feeding; quail 10, 20, 32, 22/test, pheasant 20/test, controls (both) 200 birds each. Continuous feeding tests:

Duration Of Test (Days)	Level Fed (%)	Consumed (mg/k)		Mortality (%)
		Daily	Total	
		Quail		
2	0.005	1.88	3.2	100
5	.002	1.96	10.0	100
6	.001	1.35	6.9	100
19	.0005	.38	6.7	100
7 (birds 16 da old at start)	.0005	.40	2.7	55
14	.0001	.12	1.7	21.9
120	.00005	.06	7.2	13.6
CONTROL				28.5
		Pheasant		
5	.0005	.36	2.0	100
CONTROL				31.5

c) Quail; intermittent feeding experiments at 28 day intervals:

Level (%)	Initial Feeding Test				Second Feeding Test			
	Duration (Days)	Consumed (mg/k) Daily	Consumed (mg/k) Total	Mortality (%)	Duration (Days)	Consumed (mg/k) Daily	Consumed (mg/k) Total	Mortality (%)
0.001	7	1.35	9.4	81.7	7	1.2	6.1	100
.0005	7	.38	2.7	55.2	7	.19	1.3	69.7
.00001	14	.12	1.7	20.7	14	.09	1.3	26.0
CONTROL	7,14			4.0				
	42			22.0				

d) Quail (young): Effect of endrin on growth and survival:

Weeks On Test	Control		Experimental (Endrin At 0.0001%)	
	Survival (%)	Weight (g)	Survival (%)	Weight (g)
1	96	16	85	14
2	96	26	80	24
3	96	50	80	41
4	90	70	80	55
5	82	90	78	68
6	78	110	61	80
7	78	124	49	94
8	78	130	49	110
9	78	155	44	128
10	78	163	0	—

e) Quail and Pheasant, fed endrin during growth; effects:

Level (ppm)	Duration (Days)	Mortality (%)	Consumed (mg/k) Daily	Consumed (mg/k) Total
		Quail		
50	3	100	2.5	7.5
20	8	100	2.0	16.0
10	9	100	2.0	18.0
10	10	100	1.1	11.0
10	14	100	.6	8.4
5	21	72.6	.4	8.4
1	105	70.0	.1	12.6
.5	41	40.0	.2	9.0
CONTROL	120	24.0	—	—
		Pheasant		
20	4	100	1.7	8.5
5	8	100	.6	5.0
CONTROL	103	28.0	—	—

f) Effect on reproduction; quail:

Level (%)	Eggs/Hen/Day	Fertility (%)	Hatchability (%)	Young Surviving (%) At 1 Wk	Young Surviving (%) At 3 Wks	Young Surviving (%) At 12 Wks
0.001	0.37	92.9	84.6	100	89.3	63.0
CONTROL	0.53	88.6	82.3	90	87.5	78.3

g) Effect (on quail) of feeding endrin during winter maintenance:

Level (ppm)	Duration (Days)	Mortality (%)	Consumed (mg/k) Daily	Consumed (mg/k) Total
1.0	162	8.6	.07	11.0
.5	162	10.0	.04	6.5
CONTROL	162	8.7	—	—

h) Effect of endrin on reproduction; quail, pheasant:

Level In Diet (ppm) Winter	Level In Diet (ppm) Reproduction	Mortality (%)	Av. Eggs/Hen	Fertile (%)	Hatch (%)	% Young Surviving At 2 Wks	% Young Surviving At 6 Wks
			Quail				
1.0	0	25	45	84.9	70.1	80.8	50.0
1.0	1.0	60 most prior to egg production survivors discarded	—	—	—	—	—
0	1.0	25	50	93.1	79.0	89.2	64.3
CONTROL		.25	52	89.0	83.9	88.9	83.3

h) Effect of endrin on reproduction; quail, pheasant:

Level In Diet (ppm)		Mortality (%)	Av. Eggs/Hen	Fertile (%)	Hatch (%)	% Young Surviving At	
Winter	Reproduction					2 Wks	6 Wks
			Pheasant				
0	10	100	11	81.7	40.6	37.5	31.3
0	2	0	42	89.8	47.7	97.1	91.2
0	1	0	45	92.6	56.6	91.7	91.7
0	0.5	0	40	84.9	71.3	80.0	71.4
CONTROL		0	48	86.6	57.4	94.8	89.7

6) Pharmacological, pharmacodynamical, physiological, etc:

a) Mode of action: While the essential mode of action of the cyclodiene insecticides is far from clear (and thus, a fortiori, the action of endrin), experimental animals receiving endrin at toxic levels, particularly in prolonged feeding experiments, have shown neurotoxic symptoms similar to those yielded by chlordane, aldrin, dieldrin, etc.

(1) Chickens, receiving 50, 25 ppm of endrin: Highly excitable during first week; extreme excitability to stimulus, disturbance, with nervous chirping, convulsions. Lower dosages produced correspondingly less excitability. 2825

(2) Rats, rabbits, Guinea pigs, cats, monkeys, which absorbed endrin by any route in sufficient quantity, gave signs of hyperirritability to stimulus, tremors, clonic and tonic convulsions, ataxia, dyspnoea, gasping, cyanosis. Rabbits, receiving dry endrin via the skin in toxic amounts, had convulsions. Rats, in convulsive spasm, became victims of severe self-inflicted wounds. 3120 3123 2367

(3) Lethargy and anorexia to the point of complete refusal to eat have been noted in dogs and chickens as well as emaciation, respiratory distress, tremors, twitchings, severe convulsions in dogs. 2824 2367,3120

b) Hypertrophy, with a cellular degeneration and alteration of the liver, characteristic of chlorinated hydrocarbon pathology, have been noted for endrin in all fatally poisoned as well as chronically and sub-acutely intoxicated animals. 3120 2367

(1) An evidence of profound impairment of hepatic function has been found in the elevated serum alkaline phosphatase levels of endrin-intoxicated rats. The alkaline phosphatase levels remained high even during fasting. Elevated alkaline phosphatase levels have also been associated with abnormalities of phosphorylation mechanisms. 2367

(2) Degenerative lesions of brain, kidney, adrenals have likewise been noted in endrin-poisoned, experimental animals. Survivors of single doses, (rats, mice, hamsters, Guinea pigs) subjected to vapor inhalation have yielded essentially normal tissues. 3120

(3) Increase in the relative weights of liver, kidney, brain has been noted in dogs on endrin-containing diets. 3120 3123

(4) Weight loss (with distinct sexual differences), associated in degree with the amount of endrin consumed, is reported for rats, and is, to a degree at least, independent of the lesser amounts of food consumed by endrin-receiving subjects. 2367

(5) Weight gain and growth rate have been adversely affected in rats on endrin-containing diets; emaciation has been remarked in dogs. 3120 3123

(6) Rats, receiving endrin at 25, 50, 100 ppm, are reported to have shown dysenteric symptoms, intermittent blindness, nosebleed, delayed blood clotting times.

(7) Evidence of the storage of endrin in fat and liver tissue is reported from chickens and dogs. 2824,3120

(8) Pulmonary hyperaemia and oedema have been manifested by dogs fatally poisoned by endrin. 3123

(9) Toxemic lesions, passive congestion, oedema of lungs and degeneration of livers and kidneys is reported for chickens. [2824]

c) No data appear to be available on the biochemical alteration (if any) or fate of endrin in the animal body.

7) Phytotoxicity:

a) Under proper precautions of application and formulation phytotoxic hazard is apparently low. It is stated that no injury has followed for plants given dosage levels several times greater than those normally recommended. 2812 129 2120

(1) Some damage to cucumbers and corn has been suspected.

(2) The nature of the solvent, particularly in emulsifiable concentrates, must be taken into account in phytotoxicity considerations.

8) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Blabera fusca (adult)	inj	MLD	1.3 µg/g	Dissolved in acetone and triton.	1986
Blabera fusca (adult)	inj	MTD*	2.5 µg/g	Dissolved in acetone and triton.	1986
				* = Maximum Tolerated Dose	
Chrysops discalis (adult)	Topical	LD_{50}(estimate)	9 µg/fly		2707
Chrysops discalis (adult)	Topical	LD_{90}	80 µg/fly		2707
Musca domestica (larva)	Medium	LC_{50}	125 ppm (100-160 ppm)	0.95 Fiducial Limits.	666
Oncopeltus fasciatus	Topical	LD_{50}	47 µg/g		2231

8) Toxicity for insects: (Continued)

a) Quantitave:

Insect	Route	Dose		Dosage	Remarks	
Protoparce sexta (larva)	Topical	LD$_{50}$	large	42 µg/larva		1306
			medium	2.9 µg/larva		
			small	0.51 µg/larva		1306
Protoparce sexta (larva)	Topical	LD$_{90}$	large	219 µg/larva		
			medium	6.3 µg/larva	Av. wgt. small .9(.6-1.1)g 2,3 instar.	1306
			small	6.3 µg/larva	Av. wgt. medium 2.5(1.2-4.0)g 3,4 instar.	
Protoparce sexta (larva)	or	LD$_{50}$	large	9.9 µg/larva	Av. wgt. large 5.4(4.1-7.5)g 5 instar.	1306
			small	0.11 µg/larva		
Protoparce sexta (larva)	or	LD$_{90}$	large	49.0 µg/larva		1306
			small	0.85 µg/larva		

b) Comparative toxicity for insects of endrin and other compounds:

(1) Vs. Protoparce sexta (larva): Average weight 1306

small 0.9 (0.6-1.1) g
medium 2.5 (1.2-4.0) g
large 5.4 (4.1-7.5) g
larvae

Insecticide	µg/Larva									
	Topical LD$_{50}$			Topical LD$_{90}$			Oral LD$_{50}$		Oral LD$_{90}$	
	Small	Medium	Large	Small	Medium	Large	Small	Large	Small	Large
Endrin	0.51	2.9	42	6.3	6.3	219	0.11	9.9	0.85	49
Parathion	2.8	9.9	52	12.3	64	183	15.7	—	54	—
Isodrin	3	7.6	87	56	29	490	1.1	15.3	3.1	138
Lindane	—	—	206	—	—	1235	—	209	—	398
Malathion	23.6	61	481	92	533	1276	—	365	—	1621
Dieldrin	—	—	482	—	—	2559	—	—	—	—
Aldrin	—	—	487	—	—	1359	—	—	—	—
Heptachlor	—	—	1058	—	—	4005	—	—	—	—
Toxaphene	30	32	1363	112	138	5778	—	143	—	6025
DDD	37	376	2622	367	2620	9813	22.5	878	58	3192
DDT	366	2334	$\gg$4000	1342	9887	—	158	4416	1125	28,040

(2) Vs. Musca domestica (3rd instar larva); incorporated in rearing medium; toxicity measured by % emergence from pupa as compared with controls: 666

Insecticide	LC$_{50}$ (ppm)	0.95 Fiducial Limits	
Endrin	125	100-160	
Aldrin	430	340-595	difference not significant.
Dieldrin	450	355-595	
Chlordane	1450	1100-1900	
DDT	2300	1600-3300	

(3) Vs. Chrysops discalis (adult): 2707

Insecticide	Topical LD$_{50}$ (estimate)(µg/Fly)	Topical LD$_{90}$ (µg/Fly)
Endrin	9	80
Lindane	4	35
DDT	20	250
Dieldrin	20	950
Methoxychlor	30	90
Aldrin	40	170
Heptachlor	40	200
EPN	48	120
Isodrin	60	170
Chlordane	60	650
Chlorthion	65	420
Diazinon	90	360
3-Chloro-4-methylumbelliferone, O,O-diethyl thiophosphate	90	910
Q-137	120	400
Malathion	130	330
Toxaphene	180	480

(4) Vs. Blabera fusca (adult); by injection, dissolved in acetone-triton: 1986

Insecticide	MLD < 7 days (µg/g)	Maximum Tolerated Dose 7 days (µg/g)
Endrin	1.3	2.5
Aldrin	1.3	2.6

(4) Vs. Blabera fusca (adult); by injection, dissolved in acetone-triton: 1986

Insecticide	MLD < 7 days (μg/g)	Maximum Tolerated Dose 7 days (μg/g)
Dieldrin	1.5	2.6
Isodrin	1.5	2.7
Heptachlor	1.6	5
Chlordane	8	14
Acetone-Triton control	454	1388

(5) Vs. larvae and pupae of Aëdes (principally A. dorsalis): 2282

Insecticide	% Mortality 24 Hrs At 1 ppm	
	Larvae	Pupae
Endrin	100	95
Aldrin	100	.75
DDT	87	6
Dieldrin	100	79
Isodrin	100	78.8
Control	15.2	2.4

(6) Vs. Aëdes dorsalis and Aëdes vexans: 2283

Insecticide	% Mortality 24 Hrs.					
	Larvae At				Pupae At	
	1 ppm	1:2,000,000	1:5,000,000	1:10,000,000	1:2,000,000	1:5,000,000
Endrin	100	98.9	98	98	99	61
Aldrin	100	96.9	99	95	30.4	34
DDT	100	96.9	100	98	30	8.2
Dieldrin	100	96.9	99	95	78	63
Isodrin	100	98	97	81	70	58
Toxaphene	96	93	91	84	2.3	2.7

(7) Vs. Sphenarium purpurascens on corn:

Insecticide And Concentration		Active Ingred. (lb/acre)	% Mortality After		307
			12 Hrs	24 Hrs.	
Endrin	0.5% spray	0.36	32.8 (24-40)	47.6 (43-59)	
Dieldrin	1% dust	.35	74.2 (68-80)	98.2 (96-100)	
Dieldrin	2.5% dust	.88	89.8 (87-93)	99.8 (99-100)	
Aldrin	1% dust	.32	77.8 (69-88)	97.8 (95-100)	
Aldrin	2.5% dust	.82	88.6 (83-96)	99.6 (99-100)	
BHC	1% dust	.36	86.6 (78-92)	94.2 (90-97)	
BHC	2.5% dust	.85	93 (89-98)	97 (93-100)	
Isodrin	0.5% spray	.43	83.2 (81-92	91.4 (80-96)	
Parathion	0.5% dust	.16	43.6 (36-51)	69.4 (61-80)	
Parathion	1% dust	.35	66.8 (59-80)	76 (69-84)	
Toxaphene	5% dust	1.74	26.8 (18-36)	53 (46-60)	
Toxaphene	10% dust	3.6	40.4 (36-47)	61.4 (55-69)	
Chlordane	2.5% dust	.95	32 (27-39)	46.6 (41-54)	
Chlordane	5% dust	1.8	49.6 (39-62)	63.8 (50-77)	

(8) Vs. Anasa tristis; topical application in acetone solution; laboratory tests: 3376

Insecticide	% Mortality 72 Hrs At				
	32 μg/g	64 μg/g	128 μg/g	256 μg/g	512 μg/g
Endrin	—	—	100	100	100
Parathion	100	100	100	100	100
Lindane	83.3	100	100	100	100
Aldrin	—	93.3	100	100	100
EPN	—	—	100	100	100
Heptachlor	—	83.3	90	100	100
Isodrin	—	—	90	100	100
Dieldrin	—	—	70	100	100
Chlordane	—	—	36.7	80	90
Toxaphene	—	—	16.7	66.7	82
DDT	—	—	20	30	76.7

(9) Vs. Anasa tristis; rate of action of endrin and other compounds at the lowest dosage (topical application) giving a 90% or greater mortality in 72 hrs.: 3376

Insecticide	µg/g	% Mortality In			
		12 hrs.	24 hrs.	48 hrs.	72 hrs.
Endrin	128	6.7	20	80.7	100
Parathion	6	3.3	33.3	76.7	90
Lindane	64	—	80	100	100
Aldrin	64	—	23.3	76.7	93.3
EPN	128	10	26.7	76.7	100
Heptachlor	128	10	50	80	90
Isodrin	128	0	10	63.3	90
Dieldrin	256	0	70	96.7	100
Chlordane	512	—	6.7	73.3	90

(10) Vs. Leptinotarsa decemlineata (3rd instar); endrin and other compounds: 1986
[As sprays (emulsions prepared from emulsifiable concentrates)]

Insecticide	g/100 Liters	g/Hectare	% Survival At	
			24 Hrs.	48 Hrs.
Endrin	10	72	2	0
Dieldrin	10	67	7	0
Isodrin	10	65	46	2
Aldrin	10	76	88	72
Aldrin	20	136	32	22
Heptachlor	10	76	100	80
Heptachlor	20	118	66	26
Chlordane	50	316	34	24
As dusts:	g/k			
Endrin	25	686	0	0
Endrin	12.5	468	12	0
Endrin	6	184	22	0
Endrin	3	82	78	48
Dieldrin	12.5	354	0	0
Dieldrin	6	164	8	0
Dieldrin	3	85	18	0
Isodrin	25	604	0	0
Isodrin	12.5	395	20	0
Isodrin	6	175	26	0
Isodrin	3	97	62	46
Aldrin	12.5	260	2	0
Aldrin	6	184	52	24
Aldrin	3	92	66	48
Heptachlor	50	1228	8	4
Heptachlor	22	624	38	12
Heptachlor	12.5	291	57	37
Chlordane	50	1485	1	0

(11) Effects of endrin and other insecticides on certain beneficial insect predators; laboratory tests (as dusts) with adult test insects placed on plants previously treated by the vacuum dusting process: 1404

Insecticide Dust Concentration (%)		% Mortality (24 Hrs) of		
		Collops vittatus	Hippodamia convergens	Coleomegilla maculata
Endrin	1%	27	10	18
DDT	5	38	6	32
Perthane	5	23	6	12
Strobane	5	10	18	12
Heptachlor	2.5	41	30	38
Toxaphene	10	32	12	36
Dieldrin	2	36	4	24
Parathion	2	65	78	98
Malathion	5	47	90	100
Chlorthion	5	64	82	100
Diazinon	4	37	66	100
CONTROL		11	4	0
Lowest Sig. Diff.5% level		20	24	26

(12) Endrin and other insecticides; comparative toxicity for Heliothis zea and Heliothis virescens. Toxicants as topical applications to the abdominal dorsum in methyl-ethyl-ketone solutions: 1124

Toxicant	LD_{50} (μg/g) For	
	Heliothis zea	Heliothis virescens
Endrin	17	180
Toxaphene	2000	18,000
DDD	3000	17,000
DDT	3000	6,500
Malathion	130	160
Dipterex®	30	60
Bayer 17147	40	54
Shell OS-2046	4.8	4.8

(13) In the control of economic insect pests: Cotton: Recommended for thrips, cotton leafhopper, rapid plant bug, tarnished plant bug, boll weevil, bollworm (but not for pink bollworm), leafworms, grasshoppers at 1.6 lb/emulsifiable base gallon. 2812 1996
Tobacco: Recommended for hornworms, budworms, grasshoppers, flea beetles at 1.6 lb/emulsifiable base gallon.
Sugar beets: Recommended for web worms at 1.6 lb emulsifiable base/gallon.
As 1% dusts effective on tobacco vs. budworm, flea beetles, grasshoppers. Has been used successfully as a soil insecticide in experimental control of corn rootworm for which DDT is ineffective.

9) Pharmacological, pharmacodynamical, physiological, etc.; insects:

a) No data appear to be available concerned with the specific mode of action, symptomatology, biochemical action, fate, etc., of endrin in insects. There is no reason to suspect that it differs greatly (save perhaps in degree) from its chemical congeners of the cyclopentadiene (cyclodiene) group. See aldrin, dieldrin chlordane, toxaphene and heptachlor, for some of which a little data is available. 2119 520 1441, 295 2421, 422

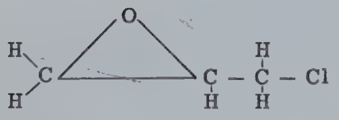
(1) For some members of this group a delayed neurotoxic action in insects, with signs resembling those of DDT, has been noted.

(2) Some workers indicate reasons for considering that the cyclodiene insecticides differ from the DDT group in their mechanism of action.

10) For screening test data (involving lice, mosquito larvae and adults, houseflies and cockroaches) consult Ref. 1801.
For labelling requirements and indication of hazard consult Refs. 2812, 3150.

82

EPICHLOROHYDRIN (1-Chloro-2, 3-epoxypropane; Chloromethyl-oxirane; γ-Chloropropylene oxide)



Molecular weight: 92.53

GENERAL

[Refs.: 2352, 1958]

An insecticidal fumigant which is essentially a chloromethyl-substituted ethylene oxide. In a survey of fumigant activity, found to be the most toxic of 100 tested substances vs. Sitophilus oryzae. A successful soil fumigant for wireworms of the genus Limonius. Highly toxic for Lucilia.

PHYSICAL, CHEMICAL

2221

Liquid; $d_4^{20^\circ}$ 1.181, $d_4^{25^\circ}$ 1.175, $d_4^{50^\circ}$ 1.144, $d_4^{75^\circ}$ 1.11; b.p. at 760 mm Hg 117.9°C, at 400 mm Hg 98°C, at 200 mm Hg 79.3°C, at 100 mm Hg 62°C, at 60 mm Hg 50.6°C, at 40 mm Hg 42°C, at 20 mm Hg 29°C, at 10 mm Hg 16.6°C, at 5 mm Hg + 5.6°C, at 1 mm Hg - 16.5°C; $n_D^{25^\circ}$ 1.43585; insoluble in water; miscible with alcohol, ether, chloroform, trichloroethylene, carbon tetrachloride; not miscible with petroleum hydrocarbons; a solvent of resins, gums, cellulose esters and ethers, paints, varnishes, lacquers and fingernail enamels.

TOXICOLOGICAL

1) Acute, subacute and chronic toxicity for higher animals:
   a) No data available to this compilation at time of preparation.

2) Phytotoxicity:
   a) Deleterious to the germination of grain. 2352

3) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Dacus dorsalis (larva)	Fumig	LC_{95} 48 hr	3.5 mg/l	2 hr exposure at 75° ± 2°F.	1537
Dacus dorsalis (naked egg)	Fumig	LC_{95} 48 hr	24.0 mg/l	2 hr exposure at 75° ± 2°F.	1537
Limonius californicus (larva)	Fumig	LC_{50}	0.8 mg/l	Relative toxicity (CS_2 = 1) 39.8 at LC_{50}.	1957
Limonius californicus (larva)	Fumig	LC_{100}	2.4 mg/l		1957
Limonius californicus (larva) Limonius canus (larva)	Fumig	LC_{50}	67.2 mg/l	5 hr exp, 77°F in 1 liter flasks with 500 g of soil.	1958
Sitophilus oryzae (adult)	Fumig	MLD_{100}	<24 mg/l	24 hr exp, ca 25°C in 500cc flasks with 250 cc wheat.	2670
Sitophilus oryzae (adult)	Fumig	LC_{100}	0.23 lb/1000 ft³	Empty vessel fumigation.	2352

a) The related compound, ethylene chlorohydrin, ($d^{20^\circ}_{4^\circ}$ 1.213, b.p. 128°C, water soluble) is reported to be very toxic for Carpocapsa pomonella (larvae) even at temperatures of 37°-40°F (3°-4.5°C). 1180

b) Comparative toxicity; epichlorohydrin and other fumigants for insects:

(1) Vs. Sitophilus oryzae (adult), in flask fumigation tests; 500 cc flasks containing 200 g (ca 250cc) wheat grain, 24 hrs exposure at ca 25°C. Fumigants giving 100% kill at minimum dosages less than 100 mg/l and deemed the most effective of 100 tested substances under the conditions of the test. Insects in contact with vapor phase only. 2670

Fumigant	MLC_{100} (mg/l)
Epichlorohydrin	<24
Ethyl mercaptan	<17
Isopropyl thiocyanate	<19
Ethyl isothiocyanate	<20
Allyl isothiocyanate	<20
Methyl disulfide	<21
tert.-Butyl bromide	<24
2-Chloroethyl ether	<24
2-Bromoethyl ethyl ether	<27
Allyl bromide	<28
2-Bromoethyl acetate	<30
Methyl bromoacetate	<30
Ethyl bromoacetate	<30
n-Propyl iodide	<35
Allyl iodide	<37
Ethyl iodide	<39
Methyl iodide	<46
Methylene iodide	<67

(2) Vs. Limonius californicus and Limonius canus, exposed for 5 hrs. in 1 liter flasks containing 500 g soil at 77°F: 1958

Fumigant	LC_{50} (mg/l)
Epichlorohydrin	67.2
Allyl isothiocyanate	2.33
Ethyl isothiocyanate	3.2
Allyl bromide	4.2
Chloropicrin	4.8
Methyl iodide	5.2
Allyl iodide	5.5
Methyl bromide	5.9
Methyl disulfide	18.8
Allyl chloride	23.5
Carbon disulfide	68.2
Allyl formate	102.2

(3) Vs. Limonius californicus: (With relative toxicities compared to carbon disulfide = 1.) 1957

Fumigant	LC_{50} (mg/l) (rounded values)	ca LC_{100} (mg/l) (rounded values)	Relative Toxicity At LC_{50} CS_2 = 1.0
Epichlorohydrin	0.8	2.4	39.8
Carbon disulfide	31.5	51	1.0
Methyl cyanide	55.8	86	.56

(3) Limonius californicus: (With relative toxicities compared to carbon disulfide = 1.) (Continued) 1957

Fumigant	LC$_{50}$ (mg/l) (rounded values)	ca LC$_{100}$(mg/l) (rounded values)	Relative Toxicity At LC$_{50}$ CS_2 = 1.0
Ethylene chloride	24.5	39.3	1.3
Ethyl formate	16.7	28.3	1.9
Diethyl carbinol	15.7	25.6	2.0
Methyl formate	12.5	23	2.5
Pyridine	5.9	15	5.3
α,β-Dichloroethyl ether	3.4	7.4	9.2
β,β′-Dichloroethyl ether	0.9	2.5	35
Crotonaldehyde	0.74	1.1-1.3	42.4
Chloropicrin	0.7	0.86	45.9
Ethylene chlorohydrin	0.24	0.6-0.8	131.9
Allyl isothiocyanate	0.16	0.21-0.24	192.9

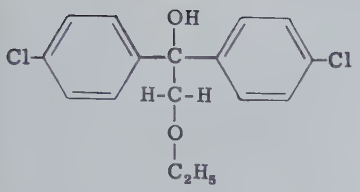
(4) Vs. naked eggs and larvae, of Dacus dorsalis; compounds whose LC$_{95}$ within 48 hrs after 2 hrs exposures at 75 ± 2°F, is <50 mg/l: 1537

Fumigant	LC$_{95}$ (mg/l)	
	Eggs	Larvae
Epichlorohydrin	24.0	3.5
Butane, 1-chloro-4-iodo-in CCl_4 2%	0.7	0.3
Butane, 1-chloro-4-iodo-in CCl_4 10%	0.3	$<$ 0.9
Methane, diiodo-	0.6	0.7
Heptane, 1-iodo-	$<$ 0.8	$<$ 0.8
Hexane, 1-iodo	$<$ 1.1	$<$ 0.7
Isothiocyanic acid, ethyl ester	4.0	1.2
Ethane, iodo-	7.0	0.3
Propene, 3-iodo-	7.2	0.8
2-Butane, 1,4-dichloro-	6.1	3.3
Cyclohexane, iodo-	7.6	2.0
Epibromohydrin	8.9	4.0
Butane, 1,2-dibromo-	8.7	7.8
Propane, 1,2-dibromo-	18.0	1.8
Crotonaldehyde	11.0	10.0
Propane, 1,3-dibromo-	5.5	18.0
Pentane, 1-iodo-	$<$ 3.9	20.0
Toluene, α-bromo	13.0	11.0
Butane, 1-iodo	$<$ 4.1	22.0
Cyclopentane, bromo-	16.0	14.0
Propane, 1-iodo-	5.5	35.0
Butane, 1-iodo-3-methyl-	14.0	31.0
Butane, 1-bromo-3-chloro-	29.0	19.0
Butylamine	13.0	38.0
Cyclopentane, chloro-	31.0	24.0
Propane, 1-iodo-2-methyl	16.0	45.0
Propane, 2-bromo-1-chloro-	39.0	28.0
Xylene, α-chloro-	27.0	43.0
Propane, 1-bromo-3-chloro-	27.0	44.0
Butane, 2-iodo	36.0	41.0

83

1-ETHOXYMETHYL-1, 1-DI-(p-CHLOROPHENYL) CARBINOL

(G 23645; Ethoxymethyl-di-(p-chlorophenyl) carbinol; Ethoxymethyl-dichlorophenyl carbinol; Etoxinol)



Molecular weight: 311.20

GENERAL

[Refs.: 1122, 898, 1287, 2230, 1810, 900, 2588, 1121]

An experimental acaricide, low in insecticidal activity and having no systemic action. In laboratory and field tests has shown excellent direct action on all stages of Metatetranychus ulmi (= Paratetranychus pilosus) and Tetranychus urticae. It is a selective acaricide with good contact toxicity for all life-cycle phases of susceptible mites, and, when tested on Vicia faba leaves, has shown residual action of ca. 1 week vs. T. urticae. Neither in laboratory or field tests has significant insecticidal potential been demonstrated. Etoxinol demonstrates again the acaricidal properties associated with two benzene nuclei, chlorinated in para-position and linked by a non-chlorinated bridging group. Etoxinol is one of a series of acaricides whose point of departure was di(p-chlorophenyl) methyl carbinol, q.v. This series has shown impressive effectiveness with moderate residual activity. In general the o, p′- and o, o′- dichlorophenyl carbinols are less effective than the p, p′- isomer. Etoxinol is closely related to another acaricide of promise, ethyl-4, 4′-dichlorobenzilate or G 23992, q.v.

Attention is directed to the general treatment titled Miticides or Acaricides in this work where tabular data, illustrating comparative toxic action of numerous acaricides vs. various mites and in diverse circumstances and experiences, are compiled.

PHYSICAL, CHEMICAL

Technical: A brown crystalline solid; m.p. 58°-59°C; b.p. 155°-157°C at 0.06 mm Hg; virtually insoluble in water; soluble in most organic solvents; undergoes hydrolysis in the presence of alkalis and strong acids.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) Of low toxicity for mammals and with little tendency for accumulation in the tissues.

Animal	Route	Dose	Dosage (mg/k)	
Mouse	or	LD_{50}	> 5000	1122,1121
Rat	or	LD_{50}	> 5000	1122,1121

2) Chronic toxicity for higher animals: No data available to this compilation at the time of preparation.

3) Phytotoxicity:
   a) Reports of the effectiveness of Etoxinol vs. Metatetranychus ulmi on espaliered apple trees as an after-flowering spray make no mention of phytotoxic effects. 1122,1121

4) Toxicity for acarines:
   a) Experiences with Etoxinol vs. Metatetranychus ulmi, Tetranychus urticae: A = Active stages, R = Resting stages, E = Eggs. 1122

Concentration (%)	% Mortality At								
	24 Hrs			3 Days			6 Days		
	A	R	E	A	R	E	A	R	E
0.1	100	0	0	100	35	15	100	100	100
0.05	100	0	0	100	46	29	100	100	100
0.01	100	0	0	100	42	19	100	100	100
for comparison - Ethyl-4,4′-dichlorobenzilate, G 23992									
0.1	100	0	0	100	37	32	100	100	100
0.05	100	0	0	100	20	16	100	100	100
0.01	100	0	0	100	25	23	100	100	98
for comparison Di-(p-chlorophenyl) methylcarbinol									
0.1	100	0	0	100	36	24	100	100	100
0.05	100	0	0	100	42	21	100	100	100
0.01	100	0	0	100	32	20	100	100	99

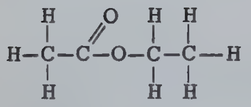
b) Etoxinol and other compounds in topical application (acetone solution), vs. Tetranychus bimaculatus ♀♀ : (Values were not characterized in the reference as µg or mg, e.g. the value for Etoxinol LD_{50} was given as .003/mite. It is assumed that mg was intended and this has been transposed to µg.) 1121

Compound	LD_{50} (??)µg/mite	LD_{50} mg/k (sic)	LD_{100} ?? µg/mite	LD_{100} mg/k (sic)
Etoxinol	3	150	7.8	390
Chlorobenzylate	2	100	3	150
DMC	4.2	210	8	400
Pyrazothion	8.2	120	1.2	60 (sic!)
Pyrazoxon	.76	3.8	.1	5 (sic!)
Diazinon	4.4	240	.2	100 (sic!)
Parathion	1.8	90	4	200
Systox	.4	20	.76	38

c) As emulsions with 0.1, 0.05, 0.01% etoxinol, directly applied to infested bean plants 100% control of Tetranychus bimaculatus was achieved. Residual action endured for 6 days; adult ♀♀ placed on > 6 day old residues laid viable eggs. 1121

84

ETHYL ACETATE (Acetic ether; Vinegar naphtha)



$\mathrm{H{-}\underset{H}{\overset{H}{C}}{-}\overset{O}{\overset{/\!/}{C}}{-}O{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}H}$

Molecular weight: 88.1

GENERAL

[Refs.: 2816, 353, 2815, 757, 1059]

Has been used, under proper circumstances, as an effective, insecticidal fumigant. A persistent residual odor restricts the use of ethyl acetate for the fumigation of such products as wheat, flour, etc. Also consult, in this work, the general treatment titled Fumigants for comparative data.

PHYSICAL, CHEMICAL

A clear, volatile, flammable liquid of fruit-like odour and pleasant taste when diluted; b.p. 77°C; m.p. -83°C; $d_4^{20°}$ 0.902, $d_{25°}^{25°}$ 0.898; $n_D^{20°}$ 1.3719; flash point + 7.2°C (open cup), lower limit of flammability in air = 2.0%, upper limit of flammability in air = 9.0%, CO_2 required to reduce flammability limits: 6.25 : 1 by volume, 3.1:1 by weight, (lbs); soluble to 1cc/10cc water at 25°C, being more soluble at lower than at higher temperatures; miscible with alcohol, acetone, chloroform, ether; absorbs water to 3.3% (w/w); solvent of varnishes, lacquers, "dopes"; vapors intensely irritating to the mucous membranes; slowly decomposed by water and moisture, becoming acid in reaction. To be kept cool, tightly closed, away from fire. 2221

a) Maximum amounts of ethyl acetate which can exist in vapor form in a 1000 ft^3 fumigating chamber at various temperatures: 2671

Temperature (°F)	V.P. (mm Hg)	Lbs/1000 ft^3
32	24	8
59	55	18
68	73	22
77	92	27
86	119	35
95	148	42
104	186	52
113	230	64
122	282	77

TOXICOLOGICAL

1) Acute toxicity for higher animals:

2221

a) Maximum allowable concentration in air = 400 ppm. 2221

Animal	Route	Dose	Dosage	Remarks	
Rat	or	LD_{50}	5620 mg/k		2907
Guinea Pig	sc	LD	3000-5000 mg/k		1043
Cat	sc	LD	ca 3000 mg/k		1043
Rat	inh	LC	57.7 mg/l, 16,000 ppm	Exposure 8 hours.	2907
Mouse	inh	LC_{50}	44 mg/l, 12,330 ppm	Exposure 3 hr, death in 3 hrs.	2931
Cat	inh	LC	61 mg/l, 17,000 ppm	Exposure 1 hr, death in 70 mins.	1044

2) Chronic toxicity for higher animals:

a) Chronic exposure results in damage to lungs, kidneys, liver, heart. 2221

3) Phytotoxicity: No data available to this compilation at time of preparation.

4) Toxicity for insects:

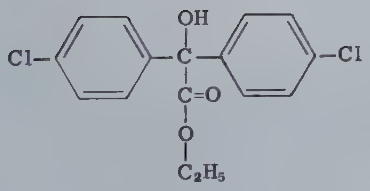
Insect	Route	Dose	Dosage	Remarks	
Cimex lectularius (adult)	Fumig	LC_{50}	25 mg/l		417
Ephestia kühniella	Fumig	LC_{50}	50 mg/l		417
Sitophilus granarius (adult)	Fumig	LC_{50}	99 mg/l		417
Sitophilus granarius (adult)	Fumig	LC_{50}	86 mg/l	Exposure 5 hr at 25°C in empty flasks.	2816, 156
Sitophilus granarius (adult)	Fumig	LC_{99}(calc)	178 mg/l	Exposure 5 hr at 25°C in empty flasks.	156
Sitophilus oryzae (adult)	Fumig	LC_{50}	36 mg/l		417
Sitophilus oryzae (adult)	Fumig	LC_{50}	49 mg/l	Exposure 5 hr at 25°C in empty flasks.	2816, 156
Sitophilus oryzae (adult)	Fumig	LC_{99}(calc)	71 mg/l	Exposure 5 hr at 25°C in empty flasks.	156
Sitophilus granarius (adult)	Fumig	LC_{50}	56 mg/l	Exposure 5 hr at 25°C 50 insects/trial;5,6 liter flasks.	984
Tineola bisselliella	Fumig	LC_{50}	69 mg/l		417
Tribolium castaneum (adult)	Fumig	LC_{50}	68 mg/l		417
Tribolium confusum (adult)	Fumig	LC_{50}	83 mg/l	Exposure 5 hr at 25°C in empty flasks.	2816, 156
Tribolium confusum (adult)	Fumig	LC_{99}(calc)	123 mg/l	Exposure 5 hr at 25°C in empty flasks.	156

5) For data indicating the comparative effectiveness of ethyl acetate with respect to numerous other fumigant compounds, consult the tabular data given in the general treatment in this work titled Fumigants.

85

ETHYL-4, 4'-DICHLOROBENZILATE

(Chlorobenzilate; Chlorobenzylate; 4, 4'-Dichlorobenzilic acid, ethyl ester; Ethyl-4,4' dichlorodiphenylglycollate; G 23992; Geigy 338.)



Molecular weight: 325.2

GENERAL

[Refs.: 1122, 898, 1287, 2230, 1810, 900, 2588, 1121, 1587]

An effective acaricide, selective and of low insecticidal power. Lacking in fumigant or systemic activity. Has given excellent direct contact action in laboratory and field tests against *Metatetranychus ulmi* (= *Paratetranychus pilosus*), and *Tetranychus urticae*. Tested against *T. urticae* on bean leaves, a residual action of ca. 1 week has been shown. Effective against all the life-cycle phases of susceptible mites. Chlorobenzilate is closely related to 1-ethoxymethyl-1, 1-di-(p-chlorophenyl) carbinol, q.v., and the comments given for that compound are apropos in the present instance. Also see the general treatment, in this work, under the title Miticides or Acaricides.

PHYSICAL, CHEMICAL

A viscous, yellowish liquid; b.p. 141°-142°C at 0.06 mm Hg; $d_{4^\circ}^{20^\circ}$ 1.28; $n_D^{20^\circ}$ 1.5727; virtually insoluble in water; soluble in most organic solvents and petroleum oils, for example, solubility in kerosene = >40% v/v; hydrolyzes in alkalis and strong acids. 1587

Formulations: As a 25% emulsifiable concentrate in xylol; a 25% water wettable powder; 3% dusts, and in a form suitable for smoke generator use.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	4850		1122,1121
Rat	or	LD_{50}	3100		1122,1121
Mouse	or	LD_{50}	729 (604-880)	Technical product; death in 48 hrs.	1587
Rat	or	LD_{50}	702 (581-848)	Technical product; death in 48 hrs.	1587
Rat	or	LD_{50}	735 (682-792)	25% xylene emulsion, death in 48 hrs.	1587

Mouse deaths: 4/5, 3/5, 4/5 at 2000, 2510, 3160 mg/k, within 48 hrs. 1587
Rat deaths: 10/10, 10/10, 9/9 at 2000, 2510, 3160 mg/k, within 48 hrs. 1587

a) Symptoms after acute application by mouth of technical product: Preening reaction, depression with salivation, lacrimation, diarrhoea, deep, rapid respiration. At high dosages: Sprawling of hind limbs, absence of righting, pain, placement reflexes. At autopsy of animals dead of poisoning: Lung haemorrhage, signs of intestinal irritation. Autopsy of survivors killed one week after receiving Chlorobenzilate®: No overt or gross pathology. 1587

b) Symptoms after acute doses of xylene emulsions: As above, plus ataxia, coma, death with intestinal irritation as pathological sign; no gross pathology in survivors of treatment. 1587

c) Symptoms following oral application as wettable powders: Depression, lacrimation, preening reaction, ataxia, rapid, labored breathing, coma, death. Autopsy of dead revealed gastro-intestinal irritation. Autopsy (after one week) of survivors: No overt pathology.

d) Single acute dermal exposures of rabbits to technical product on clipped skin under a rubber sleeve: At 0.5 cc, 1.0 cc/k no deaths, no overt pathology, save slight oedema of skin in one subject. 0.5 cc technical daily for 2 weeks, under rubber sleeve at 18 hrs per exposure: One death (probably unrelated), slight intestinal irritation. The 5 survivors showed normal weight gain with slight to mild skin irritation, erythema, slight atonia and desquamation at application site; skin returned to normal on cessation of exposure. 1587

2) Chronic toxicity for higher animals:

a) Shows only a slight tendency to accumulate in the tissues. 1122,1121

b) When fed in the diet to ♂ albino rats, 500 ppm proved to be the maximum tolerated concentration of the technical substance in prolonged exposures.

c) Weanling rats, in 2 year chronic toxicity tests: Maximum tolerated dietary level = 500 ppm without gross or microscopic pathological signs. 1587

d) Dogs tolerated Chlorobenzilate® to 64.1 mg/k/day for 35 weeks without toxic signs or gross or fine pathology. At 500 ppm in diet: Blood-tinged crusts at nose, eyes; unthriftiness, wheezing and rapid respiration; nasal discharges; exophthalmia; roughening of coat, sores, baldness; hunched-back posture. 1587

Metabolism of Chlorobenzilate®:

a) 4, 4′-Dichlorodiphenyl-methyl part of molecule was rapidly excreted in urine; no significant storage in tissues. Little or no hazard in repeated use. Rapidly absorbed and rapidly excreted by dogs in contrast to other chlorinated hydrocarbons, e.g. DDT (q.v.), which is a close analogue. 1587

3) Phytotoxicity:

a) Some foliage damage reported for pear and plum trees, and fruit injury to apple (variety: Delicious). 2120

4) Toxicity for acarines:

a) Acaricidally effective at concentrations of 0.25 lb/100 gal. U.S. 2120

b) Has been recommended, when used as a "smoke," for the tracheal mites of *Apis mellifera*. 1289

c) More effective than petroleum oil sprays vs. *Aceria sheldoni*. As summer application gave effective seasonal control of *Brevipalpus lewisi*. Has shown promise in the control of *Phyllocoptruta oleivora* and *Eotetranychus yumensis*. Less effective than either Ovotran®, q.v., or petroleum oil sprays vs. *Metatetranychus citri*. 1701

d) Comparative toxicity of Chlorobenzilate® and other compounds vs. the developmental stages of *Tetranychus bimaculatus*, placed on bean leaves (*Vicia faba*) previously treated by the settling tower method of Ebeling and Pence: 905
E = Emulsifiable Concentrate, W = Water Wettable Powder.

Acaricide		LC_{50} (g/100cc 2 days post treatment) For			
		Adult	Larva	Egg	Adult On Leaf Surface Opposite Treated Surface
Chlorobenzilate®	E	0.012	0.014	0.078	0.12
Chlorobenzilate®	W	.019	.019	.126	.22
Aramite	E	.0038	.0072	.174	.041
Aramite	W	.0041	.0082	.286	.055
DMC	E	.044	.042	.082	.21
Bis(p-chlorophenyl)ethynyl carbinol	E	.03	.033	.079	.48

Acaricide		LC$_{50}$ (g/100cc 2 days post treatment) For			
		Adult	Larva	Egg	Adult On Leaf Surface Opposite Treated Surface
Bis(p-chlorophenyl)ethynyl carbinol	W	.028	.024	.15	.88
Neotran®	W	.62	.215	.30	5.0 +
Ovotran®	E	.45	.019	.076	5.0 +
Ovotran®	W	4.25	.028	.109	5.0 +
p-Chlorophenylphenyl sulfone	E	.21	.23	.35	4.6
p-Chlorophenylphenyl sulfone	W	.27	.26	.89	5.0 +
2,4-Dichlorophenyl benzene sulfonate	E	.78	.21	.39	5.0 +
2,4-Dichlorophenyl benzene sulfonate	W	1.55	.48	.67	5.0 +
Dinitro caprylphenyl crotonate	E	.036	.013	.24	1.43
Dinitro caprylphenyl crotonate	W	.066	.027	.53	3.6
DN-111	W	.082	.031	.28	1.44
DN-289	E	.0083	.0072	.038	.24
Parathion	E	.0056	.013	.19	.021
Parathion	W	.0045	.010	.37	.027
Malathion	E	.0025	.0073	.32	.084
Malathion	W	.0042	.0115	.84	.125
EPN	E	.0025	.0047	.23	.042
EPN	W	.0048	.0077	.46	.076
Diazinon	W	.012	.028	.18	.115
Demeton (Systox®)	E	.0022	.0028	.097	.003

e) Chlorobenzilate®, Etoxinol and DMC; comparative toxicities for Tetranychus bimaculatus: 1122

A = Active Stages, R = Resting Stages, E = Eggs

Concentration (%)	% Mortality At								
	24 Hrs.			3 Days			6 Days		
	A	R	E	A	R	E	A	R	E
Chlorobenzilate									
0.1	100	0	0	100	37	32	100	100	100
0.05	100	0	0	100	20	16	100	100	100
0.01	100	0	0	100	25	23	100	100	98
Etoxinol									
0.1	100	0	0	100	35	15	100	100	100
0.05	100	0	0	100	46	29	100	100	100
0.01	100	0	0	100	42	19	100	100	100
DMC									
0.1	100	0	0	100	36	24	100	100	100
0.05	100	0	0	100	42	21	100	100	100
0.01	100	0	0	100	32	20	100	100	99

f) Chlorobenzilate® and other compounds; toxicity by topical application in acetone solution for Tetranychus bimaculatus ♀♀: 1121

Acaricide	LD$_{50}$		LD$_{100}$	
	(??) µg/mite	mg/k (sic)	(??) µg/mite	mg/k (sic)
Chlorobenzilate®	2	100	3	150
Etoxinol	3	150	7.8	390
DMC	4.2	210	8	400
Pyrazothion	2.2	120	1.2	60 (sic)
Pyrazoxon	.76	3.8	.1	5 (sic)
Diazinon	4.4	240	.2	100 (sic)
Parathion	1.8	90	4	200
Systox®	.4	20	.76	38

g) Order of effectiveness of Chlorobenzilate® and other compounds vs. Petrobia latens on dryland wheat, in lbs/acre. Based on counts made 5 days and 2 weeks after treatment: 1482

Demeton 0.5 lbs/acre > parathion 0.5 > parathion 0.25 = demeton 0.25 > Metacide® 0.25-0.5 = Schradan 0.5 > NPD 0.5-1.0 > Chlorobenzilate 0.5 = Aramite® 0.33-0.66 = Ovotran® 0.5-1.0 = Compound 923 1.0-2.0 > TEPP 0.25-0.5 = EPN 0.5 = malathion 0.75-1.5 = R-242 1.0-2.0 = toxaphene 3.0 = Compound 876 0.5 = endrin 0.15-0.3 = DMC 0.25-0.5 > BHC 0.5-1.0.

(1) Vs. Paratetranychus pratensis on wheat, Chlorobenzilate® has given erratic results. 1442

h) Chlorobenzilate®, under field conditions, has a half-life of 60-80 days on and in the peel of sprayed lemons. Does not penetrate to the juice in appreciable amounts. 1302

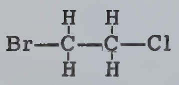
(1) Half-life values in days, Chlorobenzilate® and other compounds in citrus peel.

Acaricide; Insecticide	Half-life (Days)
Chlorobenzilate®	60-80
Aramite®	7-8
Ovotran®	10
DDT	30-40
Dieldrin	8-10
EPN	ca 80
Parathion	60-80
Sulphenone®	9-12

i) Vs. Tetranychus bimaculatus: 0.1, 0.05, 0.01% emulsions gave 100% control for all stages, with a residual action of 5 days. After > 6 days adult ♀♀ placed on residues were able to lay viable eggs. Recommended for use as a post-flowering spray characterized by brief residual activity. 1121

86

ETHYLENE CHLOROBROMIDE



$\mathrm{Br-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-Cl}$

Molecular weight: 143.43

GENERAL

One of the more recently introduced insecticidal fumigants. Useful in stored products fumigation and the fumigation of fresh fruits, etc. 2005

PHYSICAL, CHEMICAL

2005

A liquid; b.p. 107°-108°C; $d_{4°}^{19°}$ 1.689; bulk density 268 cc per lb., 14.1 lbs per gallon; specific gravity of the vapor (air = 1) 4.9; maximum weight which at 68°F can exist in vapor form in 1000 ft^3 = 12 lbs.

TOXICOLOGICAL

1) Toxicity, chronic and acute, for higher animals: No data available.

2) Phytotoxicity: No data available.

3) Toxicity for insects:
   a) Quantitative:
      (1) Toxicity for several stored products insects, exposed at 70°F to empty space fumigation in 100 ft^2 fumatoria. 2005

Insect (Adult)	2 Hour Exposure		6 Hour Exposure	
	LC_{50} 4 days (mg/l)	LC_{95} 4 days (mg/l)	LC_{50} 4 days (mg/l)	LC_{95} 4 days (mg/l)
Acanthoscelides obtectus	26	51	22	28
Oryzaephilus surinamensis	12	35	6	18
Rhizopertha dominica	15.5	37	6	19
Sitophilus granarius	23	48	3.6	16.2
Sitophilus oryzae	31	53	7.5	20.5
Stegobium paniceum	32	53	14	25
Tribolium confusum	14.5	26.5	5	18
Zabrotes pectoralis	24	40	11.5	21

(2)

Insect	Route	Dose	Dosage		
Dacus dorsalis (3rd instar)	Fumig	LC_{95} 48 hr.	2.3 mg/l, 16 g moles/l	Exposure 2 hr at 75° ± 2°F.	1536
Dacus dorsalis (naked egg)	Fumig	LC_{95} 48 hr.	< 2.2 mg/l, < 15 g moles/l	Exposure 2 hr at 75° ± 2°F.	

(3) Toxicity of ethylene chlorobromide for adult Tribolium confusum and Sitophilus granarius, exposed for 24 hrs at 80°F at various depths in whole wheat grain, in cans of 28 l capacity, 14.5 in. high, 12.5 2009

in. in diameter, holding wheat grain to a depth of 8 in. (30 lbs) with 6.5 in. of free space above the surface of the grain:

Depth of Insects in Grain (inches)	*Tribolium confusum*		*Sitophilus granarius*	
	LC_{50} (mg/l)	LC_{95} (mg/l)	LC_{50} (mg/l)	LC_{95} (mg/l)
at surface	4.5	7.6	6.6	15.9
2	5.5	20.4	11.5	22.8
5.5	19.0	28.0	16.7	39.1
	Ethylene chlorobromide + CCl_4 5 : 95			
at surface	27.9	52	30	80
2	28.2	51.8	40	85
5.5	32	68.1	52	94
	Ethylene chlorobromide + CCl_4 10 : 90			
at surface	18.1	38.3	26	50
2	20	52.1	30	64
5.5	33.9	77	43	80

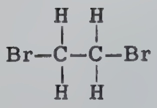
(4) Comparative toxicity: Dosages, in order of effectiveness, of various fumigants required to give 95% mortality (LC_{95}) for *Tribolium confusum*, *Sitophilus granarius*, placed at the least effective depth in wheat (5.5 in), exposure 24 hrs at 80°F. Conditions of the experiments as described in the foregoing tabulation (3): 2009

Fumigant	*T confusum*		Fumigant	*Sitophilus granarius*	
	mg/l	cc/0.5 bushel		mg/l	cc/0.5 bushel
Methyl bromide	5.3*	0.09	Methyl bromide	3.9	0.06
Acrylonitrile	19	.67	Acrylonitrile	6.8	.24
Ethylene chlorobromide	28	.46	Ethylene oxide	14.3	.45
Methylallyl chloride	29.5	.89	Methylallyl chloride	15.0	.45
Ethylene oxide	30.0	.95	1,1-Dichloro-1-nitroethane	21.7	.43
1,1-Dichloro-1-nitroethane	30.1	.59	Ethylene chlorobromide	39.1	.65
Hydrogen cyanide	39	1.6	Carbondisulfide	43.0	.95
Carbon disulfide	54	1.2	Ethylene dibromide	60.0	.77
Ethylene dibromide	56	.72	Hydrogen cyanide	60.4	2.5
Carbon tetrachloride	110*	1.9	Ethylene dichloride	> 200	> 4.46
Ethylene dichloride	111	2.5	Carbon tetrachloride	230*	4.04
Acrylonitrile 50:CCl_4 50	36	.84	Acrylonitrile 50:CCl_4 50	19	.44
Ethylene dichloride 75:CCl_4 25	59.5	1.25	Ethylene chlorobromide 10:CCl_4 90	80	1.4
Ethylene chlorobromide 5:CCl_4 95	68.1	1.3	Ethylene chlorobromide 5:CCl_4 95	94	1.65
Ethylene dibromide 5:CCl_4 95	70.0	1.2	Ethylene dibromide 5:CCl_4 95	> 113.9	> 2.0
Ethylene chlorobromide 10:CCl_4 90	77.0	1.35	Ethylene dichloride 75:CCl_4 25	> 190	> 4

* = Least effective at surface of wheat.

87

ETHYLENE DIBROMIDE (sym.-Dibromoethane; 1, 2-Dibromoethane; α,β-Dibromoethane; Ethylene bromide; EDB.)



$$\begin{array}{ccccc} & & \mathrm{H} & \mathrm{H} & \\ \mathrm{Br} & - & \mathrm{C} - & \mathrm{C} & - \mathrm{Br} \\ & & \mathrm{H} & \mathrm{H} & \end{array}$$

Molecular weight: 187.88

GENERAL

[Refs.: 539, 47, 1925, 605, 1327, 254, 2991, 2809, 1537, 1536, 3199]

An insecticidal and nematocidal fumigant of wide usefulness. Highly effective in controlling soil-inhabiting insects, for instance *Popillia japonica* and *Limonius* spp. for which uses it may be drilled into the soil in xylene or petroleum oil (light fractions) solutions, or emulsified in water for surface application, or the dipping of the root-earth mass of "balled" plants and nursery stock. Ethylene dibromide is effective in the control of more than 50 species of stored products insects, particularly those infesting stored grain or grain mills. For this use it is generally applied in mixture with other substances, viz. ethylene dichloride, q.v., carbon tetrachloride, q.v., carbon disulfide, q.v., methylene chloride, q.v., the mixtures being sprayed on the surface of binned grain. Useful in the "spot fumigation" of grain processing mills. In soil fumigation, EDB combines effectiveness with modest cost. Its movement through the soil is slow but its escape from the surface is correspondingly slow. It is effective in cold soils (ca. freezing) as well as warm. In control of *Limonius* spp., 2 gallons per acre are effective under Pacific Northwest conditions. Penetration of bagged grain and seeds in warehouses may be had with 1.5 lbs per 1000 ft^3 with a fan-agitated atmosphere. One of the most effective fumigants for dry food stuffs in atmospheric vaults. EDB has proved to be one of the more useful agents in the effective administration of plant quarantine procedures. Useful in fumigation of certain fruits and vegetables.

PHYSICAL, CHEMICAL

A heavy, colorless liquid of chloroform-like odor; m.p. ca 9°C; solidifies at 10°C; b.p. 131.7°C; $d_{4°}^{20°}$ 2.18, $d_{25°}^{25°}$ 2.172; $n_D^{20°}$ 1.5379; specific gravity as a gas (air = 1.0) 6.5; bulk density 209 cc/lb, 18.1 lb/gal. v.p. 11.0 mm Hg at 25°C 10 mm Hg at 22.7°C; maximum which can exist as a vapor at 68°F = 7 lb/1000 ft^3; soluble in water at 30° C to 0.43 parts to 100 parts w/w; soluble in most organic solvents; miscible with ether, alcohol; not flammable; chemically stable; vapors harmful!; 1 mg/l = 130.1 ppm.

Formulations: Usually formulated as a solution in inert solvents, e.g. naphtha, at a concentration of 10-42% active ingredient for soil use; in CCl_4 or other diluent for space fumigation. Examples of commercial formulations are: Dowfume W-10 and W-40, Soilfume, Bromofume, Isobrom D.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   - a) Hazard to man, animals: Far less toxic than methyl bromide. Readily absorbed via the lungs, the intact skin, the gastro-intestinal tract. Poisonous and vesicant. 1356,3199
   - b) 0.005% in air has been deemed dangerous to man. Others have considered 25 ppm to be the maximum permissible concentration for continuous exposure. 1836, 56 25 ppm have been adopted as the threshold for continuous exposure. 2711
   - c) Protective clothing, goggles, and special protective gloves (nylon,nylon-neoprene) are recommended for handlers and formulators. In emergencies, masks and air helmets are *de rigueur*. 2711
   - d) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse ♀	or	LD$_{50}$	420 (353-500)		2711
Rat ♂	or	LD$_{50}$	146 (126-170)		2711
Rat ♀	or	LD$_{50}$	117 (108-126)		2711
Rat	ct		0.25 cc	Death in 6-18 hrs.	3078,3199
Rat	inh	LC	3.08 mg/l, 400 ppm	Exposure 300 min; 20 dead/20 exposed.	2711
Rat	inh	LC	12.3 mg/l, 1600 ppm	Exposure 30 min; 20 dead/20 exposed.	2711
Rat	inh	LC	38.5 mg/l, 5000 ppm	Exposure 8.4 min; 20 dead/20 exposed.	2711
Rat	inh	LC	77.0 mg/l, 10,000 ppm	Exposure 6 min; 20 dead/20 exposed.	2711
Guinea Pig	or	LD$_{50}$	110 (98-122)		2711
Guinea Pig	inh		1.54 mg/l, 200 ppm	Exposure 420 min; 0 dead/ 15 exposed.	2711
Guinea Pig	inh	LC	3.08 mg/l, 400 ppm	Exposure 420 min; 20 dead/20 exposed.	2711
Rabbit	ct	LD	1100	Exposure 24 hrs, shaved skin, 5 dead/5 exposed; death in 4 days.	3199,2711

d) Quantitative: (Continued)

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rabbit	ct		300	2 dead/5 exposed; erythema, oedema, necrosis, CNS effects.	3199,2711
Chicken	or	LD_{50}	79 (53-117)		2711
Guinea Pig	inh	LD	0.4% v/v in air	Death within 6-18 hrs.	3078
Mouse	inh	LD	10 mg/l	Exposure 1 hr, death 5 hrs later.	3199,2756
Dog	inh	LD	50 mg/l	Exposures 15, 30, 45 mins; death within 24 hrs.	3199,2756

(1) With lower dosages death may be long delayed (rats, Guinea pigs), the fatal outcome (in as long as 12 days after exposure) being due to pneumonia, accompanied by weight loss; blood from the nose, irritability are a prelude. 2711,3199

e) Repeated, intermittent, subacute, sub-chronic, chronic toxicity; higher animals:

(1) Cats, rabbits, daily exposure 30 min/day to 0.01% concentrations in air showed: Sneezing, inflammation of nasal mucosa, salivation, trembling, some incoordination; death (rabbits 4-22 days; cats after 10 days.) 1836,3199

(2) Animals exposed to 16.5-25.5 mg/l in air, 15 min/day for 6 days showed: Irritation of eyes, nose; respiratory difficulties after each exposure; after 6th exposure paralysis of hind legs, with recovery after 13 days. 1194,3199

(3) Rats, exposed to 100 ppm 7 hrs/day showed: Steady loss of weight; 3 dead/10 exposed after 1, 5, 7 exposures; 3 dead/ 4 exposed rabbits, 2 after second, 1 after 3rd exposure, survival of one. 2711,3199

(4) Guinea Pigs exposed to 50 ppm (0.38 mg/l) 57 times in 80 days showed: Loss weight, nc mortalities. 2711,3199

(5) Rabbits, monkeys and probably rats and Guinea pigs tolerate repeated exposures of 7 hr/day, 5 day/wk to 25 ppm. Under same conditions 50 ppm is not tolerated without adverse effects. 2711,3199

(6) Rats tolerated in the diet for 4 months daily doses of 50 mg/k. 47

(7) Application to shaved skin of rabbit yielded erythema, oedema, necrosis. Instillation in the eye yielded pain, conjunctival irritation for 48 hrs, with slight surface necrosis; as 10% solutions in propylene glycol produced severe irritation for at least 48 hrs. 2711

(8) Rat, receiving orally (in oil) 40-50 mg/k/day as average daily dose showed no abnormal signs; Rat (1 animal), given 20 mg/day (total 1344 mg) was dead after 3 months, 4 Guinea pigs receiving 15 mg/ day (total 1420 mg) in 50% alcohol showed no apparent effect. 47

3) Pharmacological, pharmacodynamical, physiological, etc.:

a) After inhalation (rabbit) the tissue concentrations are reported as follows: Brain .0136%, liver .0129%, blood .0089%. 1979,3199

b) Partly broken down in mice to inorganic bromide at 0.221 mg/g in liver of animals anaesthetized by 0.75 in mM/liter. Partial elimination via lungs in unaltered form. 5,3199

c) Has moderate narcotic properties, but not for all vertebrates. 2756,2225 2049,3199

d) Central nervous effects, viz. trembling, incoordination, paralysis, irritability have been noted both in fatally poisoned as well as recovered subjects. 3199

e) Inhibits the beat of isolated frog heart in diastole at 0.00466 M, the block being reversible by saline washing. 2225

f) Vesicant effects on skin and damage to mucous membranes have been noted above. Various pathological effects include: Gastro-intestinal hemorrhage, irritation, degenerative kidney changes (convoluted tubules markedly) in Guinea pigs exposed to 50 ppm repeatedly; fatty degeneration (liver) on repeated exposure (rabbits) to 100 ppm; after inhalation lungs are hyperaemic, oedematous; pleural and pericardial exudates are reported, as well as alterations of the alveolar walls of the lungs; degenerative endothelial changes are reported. Death is attributed to pulmonary damage, circulatory failure. 3199,3078 2756,2225 1836,2711 2049

g) Signs and symptoms of intoxication in man include: Headache, prolonged vomiting, sometimes diarrhoea, weak and rapid pulse, tinnitus. Brief exposures may produce conjunctival and respiratory irritation, anorexia, headache. Skin contact may result (depending on exposure) in burning pain, erythema, inflammation, blisters. Sensitization (on repeated skin contact) is reported. 2496,3199

4) Phytotoxicity:

a) Strongly hazardous to growing plants; with slight effect only on dormant plants. When used as a soil fumigant, damage is avoided by delaying planting until 8 days after treatment. 353

b) At 100 mg/l^3, 9 months exposure, no effect on seed germination; At 200 mg/l^3 slight effect on germination potential. 47

c) Mangoes, fumigated at 16-24 ounces EDB/1000 ft^3, are unaffected in flavor, ascorbic acid content, appearance. Has been authorized for use, and has made possible the export to the U.S. of Phillipine mangoes once banned because of Anastrepha ludens. 2809

d) Decidedly less injurious than methyl bromide for certain tropical commodities and fruits which are hosts of Dacus. 1537

5) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Dacus dorsalis (larva)	Fumig	LC_{95} 48 hr	0.6 mg/l,3.2 gM/l	Exp. 2 hrs, 75° ± 2°F.	1537
Dacus dorsalis (larva) 3rd instar	Fumig	LC_{50}, LC_{95}	< 2.9 mg/l	Exp. 2 hrs, 71°-80°F, empty vessel.	255
Dacus dorsalis (naked eggs 23-26 hr old)	Fumig	LC_{50}, LC_{95}	< 2.9 mg/l	Exp. 2 hrs, 71°-80°F, empty vessel.	255
Dacus dorsalis (naked eggs)	Fumig	LC_{95} 48 hr	0.8 mg/l, 3.9gM/l	Exp. 2 hr, 75° ± 2°F.	1537
Sitophilus granarius (adult)	Fumig	LC_{50}	0.66 mg/l	Exp. 5 hr, 25°C, 5-6 l. flasks; 50/insects/trial.	984
Sitophilus oryzae (adult)	Fumig	MLC	76 mg/l	Exp. 1 hr, 20 l empty flasks.	3390
Sitophilus oryzae (adult)	Fumig	MLC	2 mg/l	Exp. 24 hr, 20 l empty flasks.	3390
Sitophilus oryzae (adult)	Fumig	MLC	109 mg/l	Exp. 24 hrs; in whole grain wheat.	3390
Sitophilus oryzae (adult)	Fumig	MLC_{100} 48 hr	87 mg/l	Exp. 24 hrs, 25°C, 500 cc flasks with ca 250 cc wheat.	2670
Tenebrioides mauritanicus (adult)	Fumig	LC_{50}	0.2 cc/5 lb corn	Exp 24 hrs, 30°C in 5 lb lots of shelled corn.	2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{50}	0.43 g/5 lb corn	" "	2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{95}	0.36 cc/5 lb corn	" "	2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{95}	0.78 g/5 lb corn	" "	2603
Tribolium confusum (adult)	Fumig	LC_{50}	14 mg/l	Exp. 5 hrs, 25°C, empty flask method.	3390
Tribolium confusum (adult)	Fumig	MLC	65 mg/l	Exp. 1 hr, 20 liter empty flask.	3390
Tribolium confusum (adult)	Fumig	MLC	3 mg/l	Exp. 24 hr, 20 liter empty flask.	3390
Tribolium confusum (adult)	Fumig	MLC	141 mg/l	Exp. 24 hrs, in whole grain wheat.	3390

(1) Toxicity of ethylene dibromide for 8 species of stored products insects, exposed at 70°F in 100 ft³ empty fumatoria; adult insects: 2005

Insect	LC_{50} (mg/l)		LC_{95} (mg/l)	
	2 Hr Exposure	6 Hr Exposure	2 Hr Exposure	6 Hr Exposure
Acanthoscelides obtectus	21.0	10.2	35.0	16.8
Oryzaephilus surinamensis	1.8	0.9	6.5	3.2
Rhizopertha dominica	3.8	3.0	10.5	6.2
Sitophilus granarius	14.0	3.0	29.0	12.0
Sitophilus oryzae	14.0	2.6	31.0	10.0
Stegobium paniceum	6.5	2.8	11.0	6.4
Tribolium confusum	12.5	3.4	21.0	7.2
Zabrotes pectoralis	5.0	2.2	9.5	5.2

(2) LC_{50}, LC_{95} dosages of ethylene dibromide for adults of Tribolium confusum, Sitophilus granarius, exposed 24 hrs. at 80°F in and on the surface of wheat grain in 28 l cans, 14.5 in. high, diameter 12.5 in., holding 30 lbs whole wheat 8 in. deep in the cans, with 6.5 in. free space above the grain; mg/l ÷ 16 = lbs/1000 ft³: 2009

Depth Of Insects In Wheat (inches)	Tribolium confusum		Sitophilus granarius	
	LC_{50} (mg/l)	LC_{95} (mg/l)	LC_{50} (mg/l)	LC_{95} (mg/l)
at surface	< 7.8	< 7.8	< 7.8	< 7.8
2	< 7.8	32.0	9.0	24.0
5.5	34.0	56.0	30.0	60.0
	Ethylene dibromide + CCl_4 5:95			
at surface	28.7	42.0	25.8	47.2
2	31.0	58.0	37.0	69.0
5.5	42.7	70.0	44.2	> 113.9

(3) Dosages (in order of effectiveness) of ethylene dibromide and other compounds required for 95% mortality (LC_{95}) of Tribolium confusum and Sitophilus granarius (adult), exposed at the least effective level (5.5 inches deep) in whole wheat grain for 24 hrs. at 80°F, the experimental apparatus being as described in the tabulation immediately preceding: (mg/l ÷ 16 = lbs/1000 ft³) 2009

Fumigant	Tribolium confusum		Fumigant	Sitophilus granarius	
	mg/l	cc/0.5 bushels wheat		mg/l	cc/0.5 bushel wheat
Methyl bromide	5.3*	0.09	Methyl bromide	3.9	0.06
Acrylonitrile	19	.67	Acrylonitrile	6.8	.24
Ethylene chlorobromide	28	.46	Ethylene oxide	14.3	.45
Methylallyl chloride	29.5	.89	Methylallyl chloride	15	.45
Ethylene oxide	30	.95	1,1-Dichloro-1-nitroethane	21.7	.43

(3) Dosages (in order of effectiveness) of ethylene dibromide and other compounds required for 95% mortality (LC_{95}) of Tribolium confusum and Sitophilus granarius (adult), exposed at the least effective level (5.5 inches deep) in whole wheat grain for 24 hrs. at 80°F, the experimental apparatus being as described in the tabulation immediately preceding: (mg/l ÷ 16 = lbs/1000 ft^3) (Continued) 2009

Fumigant	Tribolium confusum		Fumigant	Sitophilus granarius	
	mg/l	cc/0.5 bushels wheat		mg/l	cc/0.5 bushels wheat
1,1-Dichloro-1-nitroethane	30.1	.59	Ethylene chlorobromide	39.1	.65
Hydrogen cyanide	39.	1.6	Carbon disulfide	43	.95
Carbon disulfide	54	1.2	Ethylene dibromide	60	.77
Ethylene dibromide	56	.72	Hydrogen cyanide	60.4	2.5
Carbon tetrachloride	110*	1.9	Ethylene dichloride	> 200	> 4.46
Ethylene dichloride	111	2.5	Carbon tetrachloride	230*	4.04
Acrylonitrile 50:CCl_4 50	36	.84	Acrylonitrile 50:CCl_4 50	19	.44
Eth. dichloride 75:CCl_4 25	59.5	1.25	Eth.chlorobromide 10:CCl_4 90	80	1.4
Eth. chlorobromide 5:CCl_4 95	68.1	1.3	Eth.chlorobromide 5:CCl_4 95	94	1.65
Eth. dibromide 5:CCl_4 95	70.0	1.2	Eth. dibromide 5:CCl_4 95	> 113.9	> 2.0
Eth. chlorobromide 10:CCl_4 90	77	1.35	Eth. dichloride 75:CCl_4 95	> 190	> 4

* = Least effective at the surface of wheat.

6) Comparative toxicity of ethylene dibromide and other fumigants vs. diverse insects and under various experimental conditions:
   a) Consult, in this work, the tabulations under the general treatment titled, Fumigants.

7) Other considerations:
   a) Resistance to ethylene dibromide:
      (1) Resistance, manifested by certain strains ("populations") of scale insects, viz. Aonidiella aurantii, Saissetia oleae, Coccus pseudo-magnoliarum, has been reported. 2559 2560
      (2) Contrary to the foregoing, it is reported that the strain of Aonidiella aurantii which manifests resistance to methyl bromide and ethylene oxide, does not differ from the ordinary strains in its resistance to ethylene dibromide. 2007
   b) Qualitative, other appraisals:
      (1) High toxicity of ethylene dibromide as a fumigant for Tenebrioides mauritanicus is reported by some workers. 2603
      (2) High effectiveness for Popillia japonica is reported. 2134
      (3) Toxicity for Limonius californicus described. 2134
      (4) Limonius californicus, in soil, controlled by 36 lb/acre (10-20 gallons/acre) of pure ethylene bromide injected into the infested soil. 2991
      (5) Polyphylla perversa (larva), in the soil of strawberry beds, controlled by 8 gallons/acre as an emulsion with 20% ethylene dibromide. 353
      (6) Ethylene dibromide is considered slightly more effective for controlling Tribolium confusum than is ethylene dichloride, LC_{50} value 14 mg/l vs. 19 mg/l. 2816 1798
      (7) Reported to be much more toxic for Musca domestica than is ethyl bromide. 984
      (8) Vs. Anastrepha ludens on mango fruits: 2809
      Fumigation of infested mangoes at 77° ± 3°F for 2 hrs, at dosages of from 2-24 ounces/1000 ft^3 (981, 018 eggs, larvae) gave last survival at 12 ounces/1000 ft^3. % mortality in probits showed linear regression. 15 tons of mangoes were fumigated in drum fumatoria (7.4 ft^3 capacity.) 11% of the ethylene bromide, applied at 8 ounces/ 7.4 ft^3 in a 33% fruit load was recoverable.

8) No data are available on the mode of action of ethylene dibromide for insects.

9) Supplemental Data: 47
   a) Toxicity of ethylene dibromide, others for Sitophilus oryzae, Tribolium confusum; flask fumigation at 30°C in flasks of 250, 500 cc capacity:

Fumigant	LC_{50} (mg/l) For			
	4 Hours Exposure		24 Hours Exposure	
	Sitophilus	Tribolium	Sitophilus	Tribolium
Ethylene dibromide	5-8	13-17	1-2	2
Carbon disulfide	30-40	50-70	13	—
Ethylene dichloride	80-150	70-73	20-40	25
Methyl bromide	5-7	11-13	2-3	—

   b) Ratio of the LC_{100} 24 hrs in absence of and presence of absorbent (wheat) in the fumigation flasks:

Ethylene dibromide	15-10
Methyl bromide	2.5-3
Ethylene dichloride	8-12

   c) Bread baked from ethylene dibromide-fumigated flour contains < 2 mg ethylene dibromide/K bread; consumption of such bread at 0.5 K/day, without adverse effects by a 50 K man (yielding 0.02 mg ethylene Br_2/K) seems to exclude hazard. No baking abnormalities of treated flour observed.

d) Germination of wheat unimpaired after 9 months at 100 g ethylene Br_2/m^3; at 200 g/m^3, after 3 months exposure, slight impairment of germination in wheat, barley (laboratory tests), no deleterious effect in practical tests.

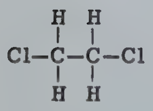
e) Absorption of ethylene dibromide by grain is ready and high; conversely penetration into stored products is rather poor. In presence of absorbing materials and stored products much larger practical concentrations must be used than laboratory toxicity data (empty chamber fumigation) might indicate. Due, however, to high toxicity and high specific gravity, relatively small volumes are needed per ton of goods fumigated. Can be applied by the inexperienced with minimum of precautions. In empty store rooms (60 m^3) 15 g/m^3 in 24 hrs. exposures yielded 100% kills of Sitophilus oryzae and Tribolium confusum. Good in airtight spaces filled with sacks where a layer of only 20 cm is to be penetrated; also good in large mechanized silos and bins where it may be mixed with grain. Also useful in grain treatment in suitable tented spaces.

Addendum; recent data on ethylene dibromide:

1) Use of ethylene dibromide in the fumigation of mangoes to control Anastrepha mombinpraeoptans: 2631
   a) Ethylene dibromide has proved highly effective vs. various fruit flies and has been highly effective vs. Anastrepha mombinpraeoptans in mangoes at 55°F. (air and fruit temperature.)
   b) In experimental tests in small chambers holding a 25% load, ethylene dibromide has been effective vs. Anastrepha at 2 ounces/1000 ft^3 in 2 hour exposures, with good tolerance on part of exposed mangoes. In practical tests effective dosages were: 4 ounces/1000 ft^3 in a 50 ft^3 chamber with a 25% load to ca 12 ounces/1000 ft^3 in a 2600 ft^3 chamber with a 40-45% load of mangoes in crates.
   c) In small scale tests, carried on in 55 gallon drums at 2 hour exposures, 52°-55°F: LD_{95} = ca. 0.75 ounce and LD_{100} = ca. 2 ounces.
   d) At temperatures down to 60°F, ethylene dibromide proved highly effective vs. Dacus dorsalis, with complete kills at 4 ounces/1000 ft^3.

88

ETHYLENE DICHLORIDE (sym.-Dichloroethane; 1, 2-Dichloroethane; α,β-Dichloroethane; Ethylene chloride; Dutch liquid.)



$Cl-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-Cl$

Molecular weight: 98.97

GENERAL

[Refs.: 539, 3199, 353, 2120, 129, 2815, 757, 1059, 605, 1327, 2260, 1502, 610, 1149, 2670, 614, 2352]

An insecticidal fumigant. Used to control a wide variety of insects as a general fumigant in buildings, warehouses, vaults, grain-elevators, etc., under conditions in which it can be safely handled. It is toxic to man and higher animals, and the breathing of the vapors is to be avoided. Also used as a soil fumigant to control such insects as Popillia japonica and Sanninoidea exitiosa. Ethylene dichloride is ordinarily mixed with other fumigants, for example ethylene dibromide, methylene chloride, carbon tetrachloride, carbon disulfide. The chief use is in the control of stored products insects and in storage places where it can be evaporated from wide surface pans placed at elevated locations or it may be sprayed directly on the surface of grain bins. Commodities having a high content of fat may keep an unpleasant smell and taste after treatment. May be used effectively as a local or spot fumigant in grain processing plants, flour mills, etc. Useful in small scale fumigation vs. clothes moth and carpet beetles.

PHYSICAL, CHEMICAL

A heavy, colorless liquid; solidifies at -35.3°C; m.p. ca -36°C; b.p. 83.5°C; $d_{4°}^{20°}$ 1.253 (as the liquid); specific gravity of the gas (air = 1.0) 3.5; $n_D^{20°}$ 1.443; v.p. 78.0 mm Hg at 25°C, 62.9 mm Hg at 20°C; flammable in contact with open flame, the flammability limits being 6.2 - 15.9% v/v in air; flash point 13.3°C (56°F) closed cup, 18.3° C (65°F) open cup; odor is chloroform-like; taste is sweetish; vapor saturation at 25°C = 430 mg/l; bulk density = 361 cc/lb, 10.5 lb/gallon; maximum which can exist as a vapor at 68°F in 1000 ft^3 = 21 lbs; virtually insoluble in water (0.9 parts : 100 parts at 0°C); soluble in most organic solvents; miscible with alcohol, ether; does not corrode metals or stain textiles; powerful solvent, damaging to rubber; solvent of fats, greases, waxes, resins, gums, "dopes", rubber; flammability hazard minimized by combination with trichloroethylene, CCl_4, CO_2; stable in water, acids, alkalis; 1 mg/l = 247 ppm, 1 ppm = 0.00405 mg/l.

Formulations: Used per se or in mixture with CCl_4 as Chlorasol, which may be applied at 8-14 lb per 1000 ft^3
in space fumigation or at 3 gal. per 1000 bushels of grain. Maximum amounts of ethylene dichloride which can 2671
exist in vapor form at various temperatures, in a 1000 ft^3 fumigating chamber:

Temperature (°F)	V.P. (mm Hg)	Lbs As Vapor/1000 ft^3
32	24	8.6
59	49	17
68	63	21
77	80	26
86	100	33
95	125	40
104	154	49
113	189	55
122	230	71

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) Considered to be relatively low in toxicity for mammals, being somewhat less toxic than or approximately 2747
   as toxic as, chloroform and carbon tetrachloride and more toxic than methylene chloride. For exposures 2315
   of from <1 hour to 1 hour about as toxic as chloroform and CCl_4; for shorter exposures less toxic.
   b) Maximum permissible concentration (continuous exposure) for man = 100 ppm, a value which has been 2934
   adopted as a threshold limit. 56,1665
   c) Toxic by ingestion, inhalation, skin contact. 146,3340,2036
   3199,2159
   d) Man is reported to experience no disturbance in short exposures at 1000 ppm; the danger level for 30 2747
   minute exposure = 5000 ppm.

Animal	Route	Dose	Dosage	Remarks	
Mouse	or	LD_{50}	910 (870-950) mg/k		2907
Mouse	inh	MLC	35 mg/l	Exposure 2 hrs.	1938
Mouse	inh	LC_{50}	150-200 mg/l;56850-75800 ppm	Exposure 2 hrs.	1938
Mouse	inh	LC_{100}	12.4 mg/l; 3000 ppm	Exposure 7 hrs; death within 1 day.	1491
Rat	or	LD_{50}	770 (670-890) mg/k		2907
Rat	sc		1 cc/k	Death of 35% of subjects at end of 24 hrs.	1525
Rat	inh	LC_{100}	12.4 mg/l; 3000 ppm	Exposure 7 hrs; death within 1 day.	1491
Rat	inh	LC_{50}	4 mg/l; 1000 ppm	Exposure 4 hrs.	480
Rat	inh	LC_{50}	12,000 ppm	Exposure ca 30 min; death in 2-7 days.	2934
Rat	inh	LC_{50}	3,000 ppm	Exposure 165 min; death in 2-7 days.	2934
Rat	inh	LC_{50}	1,000 ppm	Exposure 432 min; death in 2-7 days.	2934
Rat	inh	$LC_{0.01}$	12,000 ppm	Exposure ca 14 min.	2934
Rat	inh	$LC_{0.01}$	3,000 ppm	Exposure ca 1 hr.	2934
Rat	inh	$LC_{0.01}$	1,000 ppm	Exposure 222 min.	2934
Rat	inh	LC_0	12,000 ppm	Exposure 6 min; no harmful effect.	2934
Rat	inh	LC_0	3,000 ppm	Exposure 18 min; no harmful effect.	2934
Rat	inh	LC_0	1,000 ppm	Exposure 90 min; no harmful effect.	2934
Rabbit	or	LD_{50}	910 (860-970) mg/k		2907
Rabbit	ct	LD_{50}	3890 (3400-4460) mg/k		2907
Rabbit	sc	MLD	1600 mg/k	Given in oil solution; death in 24 hrs.	195
Rabbit	inh	LC_{100}	12.4 mg/l; 3000 ppm	Exposure 7 hrs; death 1-3 days.	1491
Guinea Pig	inh	LC_{100}	12.4 mg/l; 3000 ppm	Exposure 7 hrs; death 1-2 days.	1491
Dog	or	MLD	2500 mg/k	Given in oil solution; death in 24 hrs.	195
Dog	or		3.7 cc/k	Retching, vomiting, salivation, incoordination followed by quick recovery.	3378
Dog	iv	MLD	175 mg/k	Death in 24 hrs.	195
Dog	iv	LD	95-134 mg/k; 0.25-0.5 cc	Death in 8-24 hrs.	1819
Man	inh		4000 ppm	Exposure 1 hr produced serious illness.	2221
Guinea Pig	inh	LC	6% concentration	Symptoms in 10 min; death after 30 min.	2747
Guinea Pig	inh	LC	1% concentration	Symptoms in 15-20 min.	2747
Guinea Pig	inh	LC_0	0.12% concentration	No symptoms, no death following 8 hrs exp.	2747
Guinea Pig	inh	LC	10-20% concentration	Fatal within a few minutes.	2747
Guinea Pig	inh	LC	0.4-0.6% concentration	Dangerous to life in 30-60 min exposures.	2747
Guinea Pig	inh	Max. Td.Conc.*	0.35%	60 min. exposure; *=Maximum Tolerated Concentration.	2747

2) Subacute, subchronic and chronic toxicity; effects of repeated exposure; higher animals:
   a) 1000 ppm after a few 7 hour exposures gave death: Rats, Guinea pigs, rabbits; dogs died after several 1489
   7 hr exposures at 1000 ppm. 3199
   b) Dogs exposed daily, 7 hr/day for 8 months, at 400 ppm: Outwardly unharmed; at autopsy: Slight fatty 1489
   degeneration of liver. At 400 ppm some deaths of rats, rabbits and Guinea pigs although some survived 3199
   many exposures.

c) All animals tested tolerated repeated exposure at 100 ppm. 1489,3199
d) Maximum concentration tolerated without harmful effects, 7 hrs exposure/day, 5 days/week for 6 months: Rabbits 400 ppm; rats 200 ppm; monkeys, Guinea pigs 100 ppm. 2934,3199

3) Pharmacological, pharmacodynamical, physiological, etc.; higher animals:
a) Readily absorbed via the lungs; moderate absorption via unbroken skin (rabbit); dermatitis follows contact of human skin with ethylene dichloride. 3340 2788
b) On laboratory animals, exercises a central nervous depressant action; narcotic concentration (mouse) .00021 M/l (chloroform .00017 M/l, CCl_4 .00032 M/l); narcotic concentration for fish similar to that of chloroform. 2315 1938 1963
c) Narcosis, (dogs via inhalation) preceded by excitement, free salivation; reflexes extinguished after 2 minutes; consciousness returns in 30 minutes after establishment of complete narcosis. Narcosis of >15 minutes duration yields toxic effects. 0.5 cc/k received intravenously (dog) gave deep anesthesia, slowing of of respiration, slow heart rate, feeble heartbeat, extinction of reflexes in 8 minutes succeeded by death without return to consciousness after 6 hours; at 0.25 cc/k gave narcosis enduring 4 minutes followed by complete recovery in 20 minutes followed by death within 24 hours; at 0.125 cc gave no central nervous depression, but excitement and incoordination with later recovery. 0.3 cc/k by mouth produced temporary respiratory halt with, occasionally, Cheyne-Stokes breathing. 1819
d) Excretion of ethylene dichloride: Mainly via the lungs. Metabolic fate, if any, in organism: Unknown. 3199
e) 0.031 M/l in physiological saline brought arrest of frog heart preparations. After oral administration (dogs) blood pressure declined to a degree proportional to dosage. 1071,1819
f) Hemolytic effect on erythrocytes in vitro by ethylene dichloride solutions are known. 1789
g) Animals fatally poisoned (inhalation) showed hyperaemia and oedema of lungs, degenerative kidney changes, damage to liver, adrenal glands. 3199
h) Dogs, exposed to vapors, showed corneal opacity with visual impairment. The effect is not one of direct contact, being evocable by subcutaneous administration. 865,2435 2965,1486
i) Histopathology produced by ethylene dichloride comprises: Fatty degeneration of liver, degeneration of renal tubules, necrosis and haemorrhage of the adrenal cortex, myocardial fatty degeneration. Various dietary factors appear to influence mortality and pathology. 3378,1819 1489,2934 1491,1493,1525
j) Symptoms of intoxication in man comprise: By ingestion: Nausea, vomiting (with blood) diarrhoea, pain cramps followed by headache, ataxia, stupor, unconsciousness leading to weak and rapid pulse; cyanosis followed by death in respiratory and circulatory failure; by inhalation: Fatigue, drowsiness, headache, nervousness, tremor, anorexia, vomiting may be present and the liver may be tender and enlarged; leucocytosis, low blood pressure, slow heart beat have been noted. In fatal cases liver degeneration has been observed. 3199

4) Phytotoxicity: [3374, 353, 2860, 2133]
a) Severely phytotoxic to plants by direct contact.
b) When applied as a soil fumigant, phytotoxicity is influenced by plant species, soil type, soil moisture.
c) May predispose peach trees to winter injury.
d) No effect on germination of wheat when employed at insecticidal levels.
e) Depending upon soil and climate the peach tree may be damaged by soil applications to control the peach tree borer; on some soils peach trees tolerated 4 ounces of 30% emulsion applied around tree base.
f) Used as a turf fumigant (e.g. vs. Japanese beetle larvae) at 1 gallon/yard², as a 1% emulsion yellows grass temporarily.

5) Toxicity for insects:
a) Toxicity of ethylene dichloride for 8 species of stored products insects exposed at 70°F, in 100 f³ empty fumatoria for 2 hr. and 6 hr. exposures; adult insects: 2005

Insect	LC_{50} (mg/l)		LC_{95} (mg/l)	
	2 Hr Exposure	6 Hr Exposure	2 Hr Exposure	6 Hr Exposure
Acanthoscelides obtectus	127	49	186	83
Oryzaephilus surinamensis	122	39	130	77
Rhizopertha dominica	137	65	228	106
Sitophilus granarius	>271	127	>271	>135
Sitophilus oryzae	166	66	>271	123
Stegobium paniceum	161	77	242	128
Tribolium confusum	132	53	226	84
Zabrotes pectoralis	52	26	92	48

Insect		Route	Dose	Dosage	Remarks		
Attagenus piceus Anthrenus vorax	(larva)	Fumig Fumig	MLD	6 lb/1000 ft³	(Ethylene dichloride-CCl_4 3:1) at 85°F	24 hrs. exposure in vials buried in "overstuffed" furniture.	2670
Attagenus piceus Anthrenus vorax	(larva)	Fumig	MLD	12 lb/1000 ft³	(Ethylene dichloride-CCl_4 3:1) at 65°F		

Insect	Route	Dose	Dosage	Remarks	
Attagenus piceus (larva)	Fumig	LC_{50}	195.0 mg/l	Exp. 5 hr, at 25°C, empty flask fumigation.	2816
Bruchus obtectus (adult)	Fumig	LC_{50}	72 mg/l	Exp. 5 hr, at 25°C, empty flask fumigation.	2817
Cimex lectularius (eggs, nymphs, adults)	Fumig	LC_{95}-LC_{100}	> 50 mg/l	Exp. 5 hr, at 25°C, in empty 12 l flasks.	2622
Cimex lectularius (eggs, nymphs, adults)	Fumig	LC_{95}-LC_{100}	> 50 mg/l	Ethylene chloride-CCl_4 3:1; exp 5 hr. at 25°C, empty flask.	2622
Dacus dorsalis (naked eggs 23-26 hr old)	Fumig	LC_{50}	2.3 mg/l	Exp. 2 hrs, at 71°-80°F, empty vessel.	255
Dacus dorsalis (naked eggs 23-26 hr old)	Fumig	LC_{95}	5.9 mg/l	Exp. 2 hrs, at 71°-80°F, empty vessel.	255
Dacus dorsalis (larva 3rd instar)	Fumig	LC_{50}	38.0 mg/l	Exp. 2 hrs, at 71°-80°F, empty vessel.	255
Dacus dorsalis (larva 3rd instar)	Fumig	LC_{95}	120.0 mg/l	Exp. 2 hrs, at 71°-80°F, empty vessel.	255
Limonius californicus (larva)	Fumig	LC_{50}	24.5 mg/l	Relative toxicity (CS_2 = 1.0) = 1.3	1957
Limonius californicus (larva)	Fumig	LC_{100}	39.3 mg/l		1957
Limonius californicus *Limonius canus* } (larva)	Fumig	LC_{50}	295.2 mg/l	Exp. 5 hrs, at 77°F, in flasks containing soil.	1958
Oryzaephilus surinamensis (adult)	Fumig	LC_{50}	0.152 cc/5 lb shelled corn.	Exp. at top of container 24 hrs at 30°C.	2605
Oryzaephilus surinamensis (adult)	Fumig	LC_{50}	0.153 cc/5 lb shelled corn.	Exp. at bottom of container 24 hrs at 30°C.	2605
Oryzaephilus surinamensis (adult)	Fumig	LC_{95}	0.346 cc/5 lb shelled corn.	At top } of containers holding 5 lb shelled	2605
Oryzaephilus surinamensis (adult)	Fumig	LC_{95}	0.344 cc/5 lb shelled corn.	At bottom } corn exp. 24 hr at 30°C.	2605
Sitophilus granarius (adult)	Fumig	LC_{50}	98.9 mg/l	Exp. 5 hrs at 25°C in 5-6 l flasks, empty 50 insects/trial.	984
Sitophilus granarius (adult)	Fumig	LC_{50}	138 mg/l	Exp. 5 hr at 25°C, empty flask technique.	156,2816
Sitophilus granarius (adult)	Fumig	LC_{99}	246 mg/l	Exp. 5 hr at 25°C, empty flask technique.	156,2816
Sitophilus oryzae (adult)	Fumig	LC_{50}	80-150 mg/l	Exp. 4 hrs at 30°C, empty flask.	47
Sitophilus oryzae (adult)	Fumig	LC_{50}	20-40 mg/l	Exp. 24 hrs at 30°C, empty flask.	47
Sitophilus oryzae (adult)	Fumig	LC_{50}	31 mg/l	Exp. 5 hrs at 25°C, empty flask.	156,2816
Sitophilus oryzae (adult)	Fumig	LC_{50}	29 mg/l; 0.023 cc/l±.002	Exp. 24 hrs at 30°C, empty container.	2605
Sitophilus oryzae (adult)	Fumig	LC_{95}	45 mg/l; 0.036 cc/l	Exp. 24 hrs at 30°C, empty container.	2605
Sitophilus oryzae (adult)	Fumig	$LC_{99.99}$	67 mg/l; 0.053 cc/l	Exp. 24 hrs at 30°C, empty container.	2605
Sitophilus oryzae (adult)	Fumig	LC_{99}	137 mg/l	Exp. 5 hrs at 25°C empty flask.	156,2816
Sitophilus oryzae (adult)	Fumig	LC_{50}	32 mg/l; 0.024 cc/l±.002 }	Exposure 24 hr at 30°C, empty containers	2605
Sitophilus oryzae (adult)	Fumig	LC_{95}	56 mg/l; 0.040 cc/l }	to ethylene dichloride-CCl_4 3:1.	2605
Sitophilus oryzae (adult)	Fumig	$LC_{99.99}$	90 mg/l; 0.067 cc/l }		2605
Sitophilus oryzae (adult)	Fumig	LC_{50}	0.259 cc/5 lb shelled corn.	Exposed at top of container } 24 hr exposures at	2605
Sitophilus oryzae (adult)	Fumig	LC_{50}	0.287 cc/5 lb shelled corn.	Exposed at bottom of container } 30°C in containers	2605
Sitophilus oryzae (adult)	Fumig	LC_{95}	0.426 cc/5 lb shelled corn.	Exposed at top of container } with 5 lb shelled corn.	2605
Sitophilus oryzae (adult)	Fumig	LC_{95}	0.388 cc/5 lb shelled corn.	Exposed at bottom of container }	2605
Tenebrioides mauritanicus (adult)	Fumig	LC_{50}	0.467 cc/5 lb shelled corn.	Exposure 24 hrs at 30°C.	2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{50}	0.585 g/5 lb shelled corn.	Exposure 24 hrs at 30°C.	2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{95}	0.903 cc/5 lb shelled corn	Exposure 24 hrs at 30°C.	2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{95}	1.135 g/5 lb shelled corn.	Exposure 24 hrs at 30°C	2603
Tribolium castaneum (adult)	Fumig	LC_{50}	0.153 cc/5 lb shelled corn.	At top of container } 24 hr exposure at 30°C	2605
Tribolium castaneum (adult)	Fumig	LC_{50}	0.161 cc/5 lb shelled corn.	At bottom of container } in containers with 5 lb	2605
Tribolium castaneum (adult)	Fumig	LC_{95}	0.183 cc/5 lb shelled corn.	At top of container } lots of shelled corn.	2605
Tribolium castaneum (adult)	Fumig	LC_{95}	0.209 cc/5 lb shelled corn.	At bottom of container }	2605
Tribolium confusum (adult)	Fumig	LC_{50}	70.73 mg/l	Exp. 4 hrs at 30°C, empty flask.	47
Tribolium confusum (adult)	Fumig	LC_{50}	25 mg/l	Exp. 24 hrs at 30°C, empty flask.	47
Tribolium confusum (adult)	Fumig	LC_{50}	37.5 mg/l	Exp. 5 hrs at 25°C, empty flask.	156,2816
Tribolium confusum (adult)	Fumig	LC_{50} 20-21 da	6 mg/l	Exp. 5 hrs, static fumigation } death delayed over ca.	2629
Tribolium confusum (adult)	Fumig	LC_{95} 20-21 da	12 mg/l	Exp. 5 hrs, static fumigation } 20 day period during which viable eggs were laid.	2629
Tribolium confusum (adult)	Fumig	LC_{50} 20-21 da	9 mg/l	Exp. 5 hrs, static fumigation } using ethylene dichloride-	2629
Tribolium confusum (adult)	Fumig	LC_{95} 20-21 da	14 mg/l	Exp. 5 hrs, static fumigation } CCl_4 3:1.	2629
Tribolium confusum (adult)	Fumig	LC_{50}	19.0 mg/l	Exp. 5 hrs, empty container	1798
Tribolium confusum (adult)	Fumig	LC_{50}	46.0 mg/l	At 25°C empty container } absorption ratio = 5.	1013
Tribolium confusum (adult)	Fumig	LC_{50}	240.0 mg/l	At 25°C in presence of flour }	1013

b) Species specificity of ethylene dichloride as related to route of administration: 206

Insect	Route	Dose	Dosage	Remarks
Apis mellifera (adult worker)	Parenteral	LD_{50}	2.353 mg/g	
Apis mellifera (adult worker)	Parenteral	LD_{95}	11.37 mg/g	
Apis mellifera (adult worker)	Topical	LD_{50}	40.16 mg/g	
Apis mellifera (adult worker)	Topical	LD_{95}	105.1 mg/g	
Apis mellifera (adult worker)	"inh"	LT^{*}_{50}	48 seconds	* Lethal time for 50% kill as exposure in seconds.
Apis mellifera (adult worker)	"inh"	LT^{**}_{95}	123 seconds	** Lethal time for 95% kill as exposure in seconds.
Galleria mellonella (larva)	Parenteral	LD_{50}	3.08 mg/g	
Galleria mellonella (larva)	Parenteral	LD_{95}	24.32 mg/g	
Galleria mellonella (larva)	Enteral	LD_{50}	12.22 mg/g	
Galleria mellonella (larva)	Enteral	LD_{95}	441.3 mg/g	
Galleria mellonella (larva)	Topical	LD_{50}	(76.74) mg/g	exceeded the maximum measurable dose.
Galleria mellonella (larva)	Topical	LD_{95}		beyond the experimentally measurable amt.
Galleria mellonella (larva)	"inh"	LT_{50}	3480 seconds exposure time.	
Galleria mellonella (larva)	"inh"	LT_{95}	24,210 seconds exposure time.	
Oncopeltus fasciatus (adult)	Parenteral	LD_{50}	36 mg/g	
Oncopeltus fasciatus (adult)	Parenteral	LD_{95}	827 mg/g	
Oncopeltus fasciatus (adult)	Topical	LD_{50}	208 mg/g	
Oncopeltus fasciatus (adult)	Topical	LD_{95}	575.3 mg/g	

b) Species specificity of ethylene dichloride as related to route of administration: (continued) 206

Insect	Route	Dose	Dosage	Remarks
Oncopeltus fasciatus (adult)	"inh"	LT_{50}	3270 seconds exposure time.	
Oncopeltus fasciatus (adult)	"inh"	LT_{95}	28,974 seconds exposure time.	
Popillia japonica (larva)	Parenteral	LD_{50}	2.40 mg/g	
Popillia japonica (larva)	Parenteral	LD_{95}	27.8 mg/g	
Popillia japonica (larva)	Enteral	LD_{50}	3.669 mg/g	
Popillia japonica (larva)	Enteral	LD_{95}	59.65 mg/g	
Popillia japonica (larva)	Topical	LD_{50}	21.46 mg/g	
Popillia japonica (larva)	Topical	LD_{95}	126.8 mg/g	
Popillia japonica (larva)	"inh"	LT_{50}	32 seconds exposure time.	
Popillia japonica (larva)	"inh"	LT_{95}	306 seconds exposure time.	

(1) Order of effectiveness of the various routes based on the LD_{50}, LT_{50} values for the 4 tested insects:

Apis mellifera	"Inhalation" > parenteral > topical
Galleria mellonella	Parenteral ca = "inhalation" > enteral > topical
Oncopeltus fasciatus	"Inhalation" > parenteral > topical
Popillia japonica	"Inhalation" > parenteral > enteral > topical

c) LC_{50}, LC_{95} values for adult Tribolium confusum and Sitophilus granarius, exposed to ethylene dichloride for 24 hrs at 80°F at various depths in whole grain wheat in 28 l cans 14.5 in. high, diameter 12.5 in. holding 30 lbs whole wheat grain 8 in. deep with 6.5 in. free space above grain: 209

Depth Of Insects In Wheat (inches)	Tribolium confusum		Sitophilus granarius	
	LC_{50} (mg/l)	LC_{95}	LC_{50} (mg/l)	LC_{95}
At the surface	26	51	67.3	155
2	40.1	75	83.5	> 200
5.5	54.4	111	114	> 200
	Ethylene chloride + CCl_4 3:1			
At the surface	21.1	47	63	> 190
2	28.1	56.7	72.8	> 190
5.5	29.8	59.5	81.5	> 190

d) Toxicity of ethylene dichloride for Tribolium confusum exposed for 5 hours in empty fumigation flasks at various temperatures: 156

Temperature (°C)	LC_{50} (mg/l)	LC_{99} (mg/l)
35	40	60
30	39	57
25	38	73
20	37	87
15	60	120
10	80	140
5	62	138
0	48	78

e) Toxicity of ethylene dichloride for Tribolium confusum, exposed at 25°C for 5 hours in empty 6 l fumigation flasks; in 6 l flasks with a 2 inch layer of wheat grain; in 6 l flasks with 2 inch layer of extra fine white flour; volume of material in each case = 128 in³ with 375 cm² of exposed surface; insects exposed in cages 3 in. above grain or flour surface: 156

Absorptive Material	Concentration Of Ethylene Dichloride (mg/l)	Mortality (%)
None	19.5	12.5
None	29.2	18.7
None	30.1	37.1
None	38.9	30.4
None	40.2	61.9
None	47.9	46.9
None	50.2	79.7
None	57.5	95.8
None	68.1	98.1
Wheat	40.2	3.3
Wheat	50.2	10.0
Wheat	60.3	25.5
Wheat	80.4	72.2
Wheat	80.4	50.0
Wheat	100.5	88.7
Wheat	120.6	98.0

e) Toxicity of ethylene dichloride for Tribolium confusum, exposed at 25°C for 5 hours in empty 6 l fumigation flasks; in 6 l flasks with a 2 inch layer of wheat grain; in 6 l flasks with 2 inch layer of extra fine white flour; volume of material in each case = 125 in^3 with 375 cm^2 of exposed surface; insects exposed in cages 3 in. above grain or flour surface: (continued) 156

Absorptive Material	Concentration Of Ethylene Dichloride (mg/l)	Mortality (%)
Flour	80.4	2.6
Flour	80.4	0
Flour	160.8	14.8
Flour	160.8	7.0
Flour	321.6	58.7
Flour	321.6	46.0

f) Effect of oxygen lack (vacuum fumigation) on susceptibility of adult Tribolium confusum to ethylene dichloride vapours: 608

Vacuum (Drawn & Held) inches	O$_2$,% In Tank Atmosphere (Partial Pressure Based On Atmospheric Pressure As 100%)	Ethylene dichloride (mg/l)	% Mortality 30 min Exp. 25°C
5	17.5	75	0
10	14.0	75	0
15	10.5	75	0
17	9.1	75	0
18	8.4	75	0
19	7.7	75	0
20	7.0	75	10
21	6.3	75	10
22	5.6	75	15
23	4.9	75	45
24	4.2	75	45
25	3.5	75	50
26	2.8	75	85
27	2.1	75	100
28	1.4	75	100
29	0.7	75	100

g) Ethylene dichloride, ethylene dichloride - CCl_4 3:1(standard mixture), CCl_4 in the fumigation of Tribolium castaneum and Sitophilus oryzae at 30°C in containers holding 5 lbs. shelled whole corn: 2605

Fumigant	Insect	Exposure (Hrs)	LC$_{50}$ cc/5lbs Corn		LC$_{95}$ cc/5lbs Corn	
			Top Of Container	Bottom Of Container	Top	Bottom
CCl_4	T.castaneum	24	0.136	0.129	0.174	0.164
Ethylene Cl_2 + CCl_4 3:1	T.castaneum	24	0.247	0.250	0.370	0.316
CCl_4	T.castaneum	72	0.204	0.178	0.298	0.280
Ethylene dichloride	T.castaneum	72	0.163	0.162	0.240	0.277
CCl_4	T.castaneum	168	0.165	0.157	0.199	0.193
Ethylene dichloride	T.castaneum	168	0.153	0.161	0.183	0.209
CCl_4	S.oryzae	24	0.171	0.160	0.229	0.236
Ethylene dichloride	S.oryzae	24	0.259	0.287	0.426	0.388

Exposure at 19°-26°C in containers holding 27 lb lots of shelled corn

Fumigant	Exposure (Hrs)	Insect	Dosage			% Mortality In			
			cc/27 lbs	cc/5 lbs	Gal/1000 bu	Overspace	Top	Middle	Bottom
CCl_4	72	T.castaneum	0.93	0.17	0.51	96.7	100	100	100
Ethylene dichloride	72	T.castaneum	.93	.17	.51	8.3	13.1	46.9	49.8
CCl_4	72	T.castaneum	1.08	.20	.59	100	100	100	100
Ethylene dichloride	72	T.castaneum	1.08	.20	.59	67.3	64.7	92.2	86.4
CCl_4	72	T.castaneum	1.4	.26	.77	100	100	100	100
Ethylene dichloride	72	T.castaneum	1.4	.26	.77	87.9	82.2	96.2	98.1
CCl_4	72	S.oryzae	2.0	.37	1.1	97.8	96.7	98.5	96.0
Ethylene dichloride	72	S.oryzae	2.0	.37	1.1	94.5	95.6	98.5	95.2
Eth. Cl_2 + CCl_4 3:1	24	S.oryzae	2.0	.37	1.1	95.9	96.9	92.0	95.1
CCl_4	24	S.oryzae	3.0	.56	1.64	92.4	96.6	99.3	98.8
Ethylene dichloride	24	S.oryzae	3.0	.56	1.64	100	100	100	100
Eth. Cl_2 + CCl_4 3:1	24	S.oryzae	3.0	.56	1.64	94.8	97.8	100	99.9
CCl_4	24	S.oryzae	4.0	.74	2.19	99.2	99.8	99.5	99.8
Ethylene dichloride	24	S.oryzae	4.0	.74	2.19	100	99.7	99.6	100
Eth. Cl_2 + CCl_4 3:1	24	S.oryzae	4.0	.74	2.19	100	100	99.7	100

6) Comparative toxicity of ethylene dichloride and other fumigants for insects:
   a) N.B. In the tabulations to be found in the section of this work titled Fumigants, General Treatment are numerous indications of the comparative toxicity of ethylene dichloride vis-a-vis other fumigants for diverse insects and under various experimental conditions. Attention is drawn to these data.
   b) Toxicity for Tribolium confusum and Sitophilus oryzae, of ethylene dichloride, ethylene dibromide, methyl bromide, carbon disulfide; exposure at 30°C in empty fumigation flasks 250 and 500 cc capacity: 47

Fumigant	Sitophilus oryzae LC_{50} (mg/l)		Tribolium confusum LC_{50} (mg/l)	
	4 Hr Exp.	24 Hr Exp.	4 Hr Exp.	24 Hr Exp.
Ethylene dichloride	80-150	20-40	70-73	25
Ethylene dibromide	5-8	1-2	13-17	2
Methyl bromide	5-7	2-3	11-13	—
Carbon disulfide	30-40	13	50-70	—

   c) Dosages (in order of effectiveness) of various fumigants required to give 95% mortality of Tribolium confusum and Sitophilus oryzae exposed at the least effective level in wheat (5.5 inch depth) for 24 hrs at 80°F. Conditions of the experiments as in the heading of 5, c. mg/l ÷ 16 = lbs/1000 ft³. 2009

Fumigant	T. confusum mg/l	T. confusum cc/0.5 Bu Wheat	Fumigant	S. oryzae mg/l	S. oryzae cc/0.5 Bu Wheat
Methyl bromide	5.3*	0.09	Methyl bromide	3.9	0.06
Acrylonitrile	19	.67	Acrylonitrile	6.8	.24
Ethylene chlorobromide	28	.46	Ethylene oxide	14.3	.45
Methylallyl chloride	29.5	.89	Methylallyl chloride	15.0	.45
Ethylene oxide	30	.95	1,1-Dichloro-1-nitroethane	21.7	.43
1,1-Dichloro-1-nitroethane	30.1	.59	Ethylene chlorobromide	39.1	.65
Hydrogen cyanide	39	1.6	Carbon disulfide	43	.95
Carbon disulfide	54	1.2	Ethylene dibromide	60	.77
Ethylene dibromide	56	.72	Hydrogen cyanide	60.4	2.5
Carbon tetrachloride	110*	1.9	Ethylene dichloride	200	4.46
Ethylene dichloride	111	2.5	Carbon tetrachloride	230*	4.04
Acrylonitrile-CCl_4 50:50	36	.84	Acrylonitrile-CCl_4 50:50	19	.44
Eth. Cl_2-CCl_4 75:25	59.5	1.25	Eth. chlorobromide-CCl_4 10:90	80	1.4
Eth. chlorobromide-CCl_4 5:95	68.1	1.3	Eth. chlorobromide-CCl_4 5:95	94	1.65
Eth Br_2-CCl_4 5:95	70.0	1.2	Eth. Br_2-CCl_4 5:95	>113.9	>2.0
Eth.chlorobromide-CCl_4 10:90	77	1.35	Eth. Cl_2-CCl_4 75:25	190	>4.0

* = least effective at surface of wheat.

7) For dosages of ethylene dichloride formulations recommended for the control of various stored products insects in corn, wheat stored in steel bins consult the section titled Fumigants.

8) For sorption characteristics of ethylene dichloride in patent flour consult the section titled Fumigants.

9) Pharmacological, pharmacodynamical, physiological, etc.; insects:
   a) Little data is available.
   b) Ethylene dichloride is considered a neurotoxic narcotic which selectively penetrates the insect ventral nerve cord producing there cytolysis of the neurons. 353,2601 2600
   c) For some insects, at least, ethylene dichloride is potentiated by CO_2. 617

10) Other, miscellaneous, considerations:
   a) Ethylene dichloride 75% + CCl_4 25% at atmospheric pressure is unsatisfactory as a fumigant of cigars to control Lasioderma serricorne. 661
   b) To control Sanninoidea (= Aegeria) exitiosa in cool soils emulsions of ethylene dichloride are recommended because of volatility. 98% control may be achieved at rate of 2 ounces per tree compared to p-dichlorobenzene at 0.75 ounces per tree. Usually 0.5-0.75 ounce of 10% emulsion per tree gives 98%-100% control. 116 2912
   c) Vs. Hylemyia brassicae: Ethylene dichloride was ineffective as a soil fumigant. 659
   d) Vs. Ants in outdoor nests: Ethylene dichloride proved a suitable fumigant. 353
   e) Tribolium confusum, T. castaneum, Sitophilus oryzae are rendered more susceptible to the effects of ethylene dichloride when small amounts of CO_2 are present in the fumigating vapor. 617

11) Supplemental Data: Toxicity of Dowfume EB-5 (a grain fumigant containing CCl_4 63.6%, Ethylene dichloride 29.2%, Ethylene dibromide 7.2% w/w): 2712
   a) Acute oral toxicity; LD_{50} (mg/k):

Rat ♂	0.78	(0.69-0.89)
Rat ♀	0.55	(0.46-0.66)
Guinea Pig ♂	0.28	(0.25-0.32)
Guinea Pig ♀	0.36	(0.32-0.41)
Rabbit ♀♂	0.29	(0.22-0.38)
Chicken	0.78	(0.49-1.23)

b) Toxicity by eye contact (Rabbit):

- (1) Undiluted, yields moderate pain; conjunctival irritation, which clears in a few days without evidence of residual injury; washing promptly reduces irritation. At 10% in propylene glycol a more severe response: Irritation within 2 hrs., persisting for 48 hrs. before beginning of subsidence. No permanent effect on vision. At 1% in propylene glycol: Slight pain, irritation; no corneal injury.
- (2) Toxicity by skin contact (sleeve method); rabbit:
  - (a) Repeated contact gave slight irritation, mild erythema and exfoliation.
  - (b) Repeated contact (under bandage) gave severe local burns; intense erythema, oedema, blistering skin changes.

Dowfume EB-5 by Dermal Contact (g/k)	Exposures (No.)	Rabbits (No.)	Dead (No.)
0.3	24	5	0
.5	24	5	1
.7	24	10	1
1.0	24	5	1
1.7	24	4	4

c) Feeding of grain freshly fumigated with Dowfume EB-5 at 4 gals/1000 bu for 42-44 hrs. and 4 gals/1000 bu for 10 days:

- (1) No hazard is indicated for such domestic animals as chickens, pigs, cattle, although aeration of the treated grain is recommended.
- (2) 0.5 ounce by mouth, it is suggested, might endanger human life.

d) Inhalation of Dowfume EB-5 vapors:

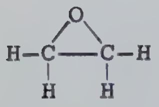
- (1) At high concentration yields anaesthesia, CNS depression.
- (2) At sufficient dosages yields liver and kidney damage similar to that caused by ethylene Cl_2 and ethylene Br_2 as well as liver injury similar to that characteristic of CCl_4.

e) Toxicity of vapors as tested by single exposures of rats:

Concentration		Exposure	Number Of	Number Of Animals
ppm	mg/l	(hrs)	Animals	Dead
9720	53.3	.5	20	20
9720	53.3	.4	20	18
9720	53.3	.35	20	6
9720	53.3	.25	20	1
9720	53.3	.2	20	0
5040	27.6	1.0	20	20
5040	27.6	.85	20	15
5040	27.6	.75	20	13
5040	27.6	.63	20	3
5040	27.6	.5	20	1
5040	27.6	.4	20	0
2450	13.4	2.0	20	20
2450	13.4	1.5	20	17
2450	13.4	1.35	20	4
2450	13.4	1.2	20	4
2450	13.4	1.0	19	0
920	5.0	7	20	20
920	5.0	6	20	19
920	5.0	5	20	16
920	5.0	4.5	20	7
920	5.0	4	18	1
920	5.0	3	19	0
480	2.6	6	20	1

89

ETHYLENE OXIDE (1, 2-Epoxyethane; Oxirane.)



Molecular weight: 44.05

GENERAL

[Refs.: 353, 2815, 757, 1059, 2120, 129, 539, 605, 1327, 436, 1221, 613, 3387, 2499]

An insecticidal fumigant which combines marked toxicity for insects, high effectiveness for the treatment of stored products, for instance, packaged cereals, rice in bags, tobacco, furs and clothing in vaults, and the desirable attribute of leaving no flavor, odor, or harmful residue in the treated material. Grains, fumigated by ethylene oxide, are not altered or damaged in their milling qualities. The vapors are deleterious to man and higher animals. Ethylene oxide also possesses important fungicidal properties which are made use of in the protection of spices from various molds. It is one of the fumigants most used in vacuum vault fumigation, being employed, ordinarily, as a 1:9 mixture with CO_2 to minimize the decided explosive hazard of air-ethylene oxide mixtures. Ethylene oxide has been found valuable in killing adult Popillia japonica (Japanese beetle) in blueberries, blackberries, raspberries, strawberries coming from infested areas. A mixture of ethylene oxide and CO_2 is effective in the control of Lasioderma serricorne by the vacuum fumigation of tobacco and tobacco products e.g. cigars. Useful in the fumigation of papers and documents, in historical archives. Among the disadvantages are the explosive hazard and a tendency to injure some fresh fruits, for example raspberries, bananas, blackberries and nuts and dried fruits. The germination potential of fumigated grains may likewise be adversely affected by ethylene oxide. Not to be confused with vinyl ether, $(CH_2{:}CH)_2O$, which is also by some called ethylene oxide. Recommended to be used in commercial fumigation at 2 lbs per 1000 ft^3. Reported to possess excellent powers of penetration, with insects buried in "overstuffed" furniture, jars of rice, and sealed cereal packages being killed with ease. In fumigation vault tests (500 ft^3 vaults), the following insects in cotton stoppered vials, exposed for 20 hours to a concentration of 1 lb/1000 ft^3 suffered 100% mortality: Tineola bisselliella, Attagenus piceus, Anthrenus vorax, Sitophilus oryzae, Plodia interpunctella, Oryzaephilus surinamensis, Necrobia rufipes, Tribolium confusum.

PHYSICAL, CHEMICAL

A gas at ordinary and room temperatures, a colorless, volatile liquid at $<12°C$; m.p.-111.3°C; b.p. 10.7°C; $d_4^{7°}$ 0.887; specific gravity of the gas, (air = 1) 1.5; $n_D^{8.4°}$ 1.3597; v.p. 760 mm Hg at 10.7°C, 1095 mm Hg at 20°C, $\gg$ 760 mm Hg at 25°C; vapor saturation at 25°C = 1800 mg/l; maximum quantity which can exist as a vapor at 68°F in a 1000 ft^3 fumigating chamber = 14 lbs; bulk density = 511 cc/lb, 7.4 lb/gallon; flammable and explosive in air at concentrations of 3-80%; miscible with water and with most organic solvents; powerful solvent of fats, oils, greases, waxes and particularly of rubber; relatively non-corrosive to materials other than rubber; highly reactive chemically yet relatively stable in aqueous solution; odor: Pleasant; vapors harmful; containers to be kept tightly closed. 613

Formulations: Ethylene oxide 90%, CO_2 10%; 20% by weight in ethylene dichloride. 2 lbs/1000 ft^3 will eliminate all insect life provided the fumigated space is tightly closed for 24 hours. The 9:1 CO_2-ethylene oxide mixture is sometimes known as Carboxide, a trade designation.

a) Recently reported to impair the nutritional qualities of treated rat diets. Stated to destroy thiamine and possibly other essential factors in stock diets. Supplementation of the treated diets with vitamin mixtures is said not to restore their growth promoting qualities. 101

b) Maximum amount of ethylene oxide which, at various temperatures, can exist in vapor form in a 1000 ft^3 fumigating chamber: 2671

Temperature (°F)	V.P. (mm Hg)	Lbs/1000 ft^3 As A Vapor
32	316	51
59	760	116
68	760	114
77	760	113
86	760	111
95	760	109
104	760	107
113	760	105
122	760	104

1 mg/l = 556 ppm; 1 ppm = 0.0018 mg/l 2815

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) Hazard:

(1) Less toxic than sulfur dioxide; dangerous dose for animals = 3000 ppm exposure 30-60 minutes. 250 ppm does not lead to any serious disturbance. 353

(2) Vapor concentration of 5000-100,000 ppm kills most animals in a short time. 129

(3) Maximum tolerated concentration (based on Guinea pigs, and signifying tolerable without serious symptoms although slight symptoms may occur) = 5.4 mg/l for 60 minutes, 0.45 mg/l for 8 hours; probable safe concentration for indefinite exposure = 0.45 mg/l, 250 ppm. 1665

(4) Maximum allowable concentration for daily 8 hour exposure = 100 ppm in air v/v. 55

(5) 3000 ppm tolerated by man for a maximum of 60 minutes; 50,000-100,000 ppm. fatal to man in a few minutes. 2221

(6) Produces an intense irritation to eyes and nose which makes it self warning.

(7) Not highly toxic to man; produces cyanosis (counteracted by CO$_2$) on long inhalation. 613

Animal	Route	Dose	Dosage	Remarks	
Cat	sc	LD	100 mg/k	Death in 10-12 hrs.	1556
Dog	iv	LD	444 mg/k (0.5 cc)	As a 20% solution in saline.	2964
Rat	inh	LC$_{50}$	7.2 mg/l; 4000 ppm	Exposure 4 hours.	480
Rat	inh	LC	104 mg/l; 58,000 ppm	Exposure 6 hours; death in 6 hours.	1481
Rat	inh	LC	180 mg/l; 100,000 ppm	Exposure 39 minutes; death within 24 hrs.	2964
Rat	inh	LC	450 mg/l; 250,000 ppm	Immediate death.	2964
Guinea Pig	inh	LC	90-180 mg/l; 50,000-100,000 ppm	Continuous exposure; death in a few min.	3213
Guinea Pig	inh	LC	36 mg/l; 20,000 ppm	1 1/2 hr exposure; death within 24 hrs.	1839
Guinea Pig	inh	LC	9 mg/l; 5000 ppm	Exposure 1 hr; death in 40 hrs.	1839

(8) In contact with the skin ethylene oxide may cause skin "burns".

b) Symptoms of intoxication in presence of appreciable amounts of ethylene oxide comprise: Eye, nose irritation, bloody, frothy, serous exudate from nose; unsteadiness, staggering gait, inability to stand upright; respiratory disturbances, dyspnoea, gasping, collapse. Not to be inhaled repeatedly or taken internally. 2221

2) Phytotoxicity:

a) Phytotoxic to plants as such. Never used on foliage or growing plants. 2816

b) Seriously impairs the germination of wheat, other grains and seeds. 2816

c) Marked toxic and lethal action on the soil microflora.

d) 2 lbs/1000 ft^3 (32 mg/l) safe on fresh fruits, except bananas, which are severely injured at such concentrations. Leaves no taint. 613,2424

e) Injurious to fruit and foliage of citrus trees when used against scale insects at 2.4% v/v, 25°C, 45 minutes exposure, which gave 100% kill of Chrysomphalus aurantii. 669

3) Toxicity for insects: (Also consult in this work the section titled, Fumigants, General Treatment, for comparative toxicity, other data)

a) Quantitative:

(1) Toxicity of ethylene oxide for 8 species of stored products insects exposed at 70°F in 100 ft^3 empty fumatoria for periods of 2 and 6 hours; adult insects: 2005

Insect	LC$_{50}$ (mg/l)		LC$_{95}$ (mg/l)	
	2 Hr Exposure	6 Hr Exposure	2 Hr Exposure	6 Hr Exposure
Acanthoscelides obtectus	13.5	10.5	49	30
Oryzaephilus surinamensis	14.5	4	29.5	10
Rhizopertha dominica	14.7	6.2	33	11.6
Sitophilus granarius	21	13.5	31	24.5
Sitophilus oryzae	14	5.4	18.5	10.4
Stegobium paniceum	14	9	22.5	13
Tribolium confusum	>40	27.5	>40	37.5
Zabrotes pectoralis	12.7	6	20.5	11

Quantitative Data for Various Insects:

Insect	Route	Dose	Dosage	Remarks	
Anthrenus vorax (larva)	Fumig	MLC_{100}	1 lb/1000 ft^3	Exp 24 hr at 75°F in 500 ft^3 vault.	2670
Attagenus piceus (larva)				Insects buried in "overstuffed" furniture.	2670
Attagenus piceus (larva)	Fumig	LC_{50}	17.0 mg/l	Exp 5 hr, 25°C empty flask.	2817
Chrysomphalus aurantii	Fumig	ca LC_{100}	2.4% v/v in air	Exp 45 min, 25°C, laboratory tests injury to	669
Chrysomphalus aurantii	Fumig	ca LC_{80}	.8% v/v+.9 mg/l HCN	Exp 30 min, 25°C, laboratory tests citrus foliage.	669
Chrysomphalus aurantii	Fumig	ca LC_{80}	.8% v/v+.9 mg/l HCN	16% survival laboratory tests. Exp 30 min, 25°C.	669
Cimex lectularius (egg)	Fumig	LC_{50} 5 da	0.242 mg/l	Exp 5 hr, 25°C in 6.4 l empty flasks.	1292
Cimex lectularius (egg)	Fumig	LC_{95-100}	<2 mg/l	Exp 5 hr, 25°C in 12 l empty flasks.	2622
Cimex lectularius (2, 3 instar)	Fumig	LC_{50} 48 hr	1.29 mg/l	Exp 5 hrs, 25°C, in 6.4 l empty flasks.	1292
Cimex lectularius (older nymphs)	Fumig	LC_{95-100}	14 mg/l	Exp 5 hrs, 25°C, in 12 l empty flasks.	2622
Cimex lectularius (adult)	Fumig	LC_{50} 48 hr	1.803 mg/l	Exp 5 hrs, 25°C, in 6.4 l empty flasks.	1292
Cimex lectularius (adult)	Fumig	LC_{50}	6.6 mg/l	Exp 5 hrs, 25°C.	412
Cimex lectularius (adult)	Fumig	LC_{50}	26 mg/l		416
Cimex lectularius (adult)	Fumig	LC_{95-100}	6-10 mg/l	Exp 5 hrs, 25°C, in 12 l empty flasks.	2622
Cimex lectularius (adult)	Fumig	LC_{99}	12.3 mg/l	Exp 5 hrs, 25°C empty flasks.	412
Cimex lectularius (egg)	Fumig	LC_{95-100}	<25 mg/l	Exp. 5 hrs, 25°C, in 12 l empty flasks with ethylene oxide + ethylene dichloride 1:3.	2622
Cimex lectularius (older nymphs)	Fumig	LC_{95-100}	35 mg/l		2622
Cimex lectularius (adult)	Fumig	LC_{95-100}	25-30 mg/l		2622
Dacus dorsalis (naked eggs 23-26 da old)	Fumig	LC_{60}	6.2 mg/l	Exp 2 hrs, 71°-80°F, empty vessel.	255
Dacus dorsalis (naked eggs 23-26 da old)	Fumig	LC_{95}	12.0 mg/l	Exp 2 hrs, 71°-80°F, empty vessel.	255
Dacus dorsalis (larva, 3rd instar)	Fumig	LC_{50}	8.7 mg/l	Exp 2 hrs, 71°-80°F, empty vessel.	255
Dacus dorsalis (larva, 3rd instar)	Fumig	LC_{95}	17.0 mg/l	Exp 2 hrs, 71°-80°F, empty vessel.	255
Ephestia kühniella (larva)	Fumig	LC_{50}	26 mg/l		416
Ephestia kühniella (larva)	Fumig	LC_{100}	80 mg/l	Exp 30 min at 760 mm Hg.	608
Ephestia kühniella (larva)	Fumig	LC_{100}	35 mg/l	Exp 30 min at a vacuum held at 29 inches.	608
Oryzaephilus surinamensis (adult)	Fumig	LC_{50}	7.5 mg/l	Exp 5 hrs, 25°C, empty vessel.	2817
Sitophilus granarius (adult)	Fumig	LC_{50}	5.5 mg/l	Exp 5 hrs, 25°C, empty vessel.	412
Sitophilus granarius (adult)	Fumig	LC_{50}	5.6 mg/l	Exp 5 hrs, 25°C, empty flask.	2816, 156
Sitophilus granarius (adult)	Fumig	LC_{50}	17 mg/l		416
Sitophilus granarius (adult)	Fumig	LC_{99}	8.4 mg/l	Exp 5 hrs, 25°C, empty vessel.	412
Sitophilus granarius (adult)	Fumig	LC_{99}	11.2 mg/l	Exp 5 hrs, 25°C, empty flask.	2816, 156
Sitophilus oryzae (adult)	Fumig	LC_{50}	5.7 mg/l	Exp 5 hrs, 25°C, empty flask.	2816, 156
Sitophilus oryzae (adult)	Fumig	LC_{50}	2.9 mg/l	Exp 5 hrs, 25°C.	412
Sitophilus oryzae (adult)	Fumig	LC_{50}	12 mg/l		416
Sitophilus oryzae (adult)	Fumig	LC_{99}	7.5 mg/l	Exp 5 hrs, 25°C, empty flask.	2816, 156
Sitophilus oryzae (adult)	Fumig	LC_{99}	4.1 mg/l	Exp 5 hrs, 25°C, empty vessel.	412
Sitophilus oryzae (adult)	Fumig	LC_{100}	48 mg/l	Exp 30 min, at 760 mm Hg, empty vessel.	608
Sitophilus oryzae (adult)	Fumig	LC_{100}	24 mg/l	Exp 30 min, in a vacuum held at 29 inches.	608
Tineola bisselliella (larva)	Fumig	MLC_{100}	1 lb/1000 ft^3	In 500 ft^3 vault, 75°F, 24 hr exp buried in "overstuffed" furniture	2670
Tineola bisselliella (larva)	Fumig	LC_{50}	18 mg/l		416
Tribolium castaneum (adult)	Fumig	LC_{50}	13.44 mg/l	Exposure 5 hrs, maximum effect when gas mixture contains 20% CO_2.	1732
Tribolium castaneum (adult)	Fumig	LC_{50}	16.6 mg/l	Exp 5 hrs, 25°C, empty vessel.	412
Tribolium castaneum (adult)	Fumig	LC_{50}	41 mg/l		416
Tribolium castaneum (adult)	Fumig	LC_{99}	27.0 mg/l	Exp 5 hrs, 25°C, empty vessel.	412
Tribolium castaneum (adult)	Fumig	LC_{100}	17.5 mg/l	Exp 5 hrs, 25°C, maximum effect when gas mixture contains 20% CO_2.	1732
Tribolium confusum (adult)	Fumig	ca LC_{50}	<20 mg/l	Exp 5 hrs, 25°C, static fumigation.	2629
Tribolium confusum (adult)	Fumig	LC_{50}	18 mg/l	Exp 5 hrs, 25°C, empty flask.	2816, 156
Tribolium confusum (adult)	Fumig	LC_{50}	15.5 mg/l	25°C, 760 mm Hg empty vessel with no absorbent present.	1013
Tribolium confusum (adult)	Fumig	LC_{50}	96 mg/l	25°C, 760 mm Hg in presence of flour, absorption ratio = 6.	1013
Tribolium confusum (adult)	Fumig	LC_{50}	18 mg/l	Exp 5 hr, 25°C at low humidity $<10\%$ R.H. at high humidity 50-70% R.H.	2008
Tribolium confusum (eggs)	Fumig	LC_{50}	2 mg/l	Exp 5 hr, 25° C at low humidity $<10\%$ R.H. at high humidity 50-70% R.H.	2008
Tribolium confusum (adult)	Fumig	ca LC_{95}	<25 mg/l	Exp 5 hrs, 25°C, static fumigation.	2629
Tribolium confusum (adult)	Fumig	LC_{99}	31.2 mg/l	Exp 5 hrs, 25°C, empty flask.	2816, 156
Tribolium confusum (pupa)	Fumig	LC_{100}	141 mg/l	Exp 30 min at 760 mm Hg, empty vessel.	608
Tribolium confusum (pupa)	Fumig	LC_{100}	22 mg/l	Exp 30 min in a vacuum held at 29 inches.	608

(2) Susceptibility to ethylene oxide of Tribolium life cycle stages, order from most to least susceptible: Egg > larva > adult > pupa. 2003

(3) Effect of certain factors on susceptibility of Tribolium confusum adults to ethylene oxide; exposure 30 min; at 86°F, ethylene oxide 16 mg/l: 608

Holding Temp. Before Fumigation (°F)	% Mortality			
	Ordinary Method	Addition 30 lb CO_2/1000 ft^3	O_2 reduced to 0.7% of 1 atmosphere	CO_2 addition + O_2 reduction
75	0	36	50	100
50	—	—	—	20

Tribolium confusum, T. castaneum, Sitophilus oryzae are more susceptible to ethylene oxide if small amounts of CO_2 are added to the fumigant medium. 617

(4) Exposure times necessary for 50% and 100% mortality (LC_{50}, LC_{100}) of Tribolium castaneum, treated with a selected concentration of ethylene oxide (17.5 mg/l) and various concentrations of CO_2; methyl formate, methyl bromide included for comparison: * 1732

%CO_2 In The Gas Mixture	Exposure Time (Hr : Min) For 50%, 100% Kills					
	Ethylene Oxide 17.5 mg/l		Methyl Formate 25 mg/l		Methyl Bromide 8.75 mg/l	
	50% Kill	100% Kill	50% Kill	100% Kill	50% Kill	100% Kill
0	2 : 30	5 : 00	2 : 30	5 : 00	3 : 40	5 : 00
1	2 : 30	5 : 00	2 : 05	3 : 30	3 : 10	4 : 30
5	1 : 22	3 : 00	: 45	2 : 00	2 : 25	4 : 00
10	: 36	1 : 30	: 25	1 : 30	2 : 05	3 : 00
20	: 22	: 45	: 19	: 45	1 : 40	3 : 00
40	: 22	: 45	: 17	: 45	1 : 50	3 : 00
60	: 17	: 45	: 17	: 45	2 : 20	3 : 30
80	: 22	: 45	: 17	: 45	2 : 25	4 : 00
99.8	: 22	: 45	: 17	: 45	3 : 10	4 : 30

The maximum insecticidal effect of ethylene oxide is achieved in the presence of 20% CO_2 in the gas mixture.

* LC_{50}, LC_{100} of the three fumigants in mg/l for 5 hrs exposures at 25°C:

Ethylene oxide	LC_{50} = 13.44	LC_{100} = 17.5
Methyl formate	LC_{50} = 17.81	LC_{100} = 25.0
Methyl bromide	LC_{50} = 6.13	LC_{100} = 8.75

(5) Dosages of ethylene oxide required to yield 50% and 95% mortality (LC_{50}, LC_{95}) for Tribolium confusum and Sitophilus granarius, exposed for 24 hrs, 80°F, at various depths in 28 l cans 14.5 in. high, diameter 12.5 inches containing 30 lbs whole grain wheat at a depth of 8 inches, with 6.5 in. free space above the grain surface: 2009

Depth At Which Insects Were Exposed In Wheat (inches)	T. Confusum		Sitophilus granarius	
	LC_{50} (mg/l)	LC_{95}	LC_{50} (mg/l)	LC_{95}
At surface	16.1	23.1	8.2	12.2
2	19	27.6	9	12.6
5.5	22.7	30	10.4	14.3

(6) Dosages (in order of effectiveness) of various fumigants to give 95% mortality at the least effective level in wheat (5.5 inches) Tribolium confusum, Sitophilus granarius exposed 24 hrs. at 80°F under experimental conditions described in the preceding table: 2009

Fumigant	For 95% Kill Of T. confusum	
	mg/l	cc/ 1/2 bushel wheat
Methyl bromide	5.3*	0.09
Acrylonitrile	19	.67
Ethylene chlorobromide	28	.46
Methylallyl chloride	29.5	.89
Ethylene oxide	30	.95
1, 1-Dichloro-1-nitroethane	30.1	.59
Hydrogen cyanide	39	1.6
Carbon disulfide	54	1.2
Ethylene dibromide	56	.72
Carbon tetrachloride	110*	1.9
Ethylene dichloride	111	2.5
Acrylonitrile + CCl_4 1:1	36	.84
Eth Cl_2 + CCl_4 3:1	59.5	1.25
Eth.chlorobromide + CCl_4 5:95	68.1	1.3
Eth.Br_2 + CCl_4 5:95	70	1.2
Eth.chlorobromide + CCl_4 1:9	77	1.35

Fumigant	For 95% Kill Of S. granarius	
	mg/l	cc/ 1/2 bushel
Methyl bromide	3.9	0.06
Acrylonitrile	6.8	.24
Ethylene oxide	14.3	.45
Methylallyl chloride	15	.45
1, 1-Dichloro-1-nitroethane	21.7	.43
Ethylene chlorobromide	39.1	.65
Carbon disulfide	43	.95
Ethylene dibromide	60	.77
Hydrogen cyanide	60.4	2.5
Ethylene dichloride	> 200	> 4.46
Carbon tetrachloride	230*	4.04
Acrylonitrile + CCl_4 1:1	19	.44
Eth. chlorobromide - CCl_4 1:9	80	1.4
Eth. chlorobromide - CCl_4 1:19	94	1.65
Eth. BR_2 + CCl_4 1:19	> 113.9	> 2.0
Eth. Cl_2 + CCl_4 3:1	> 190	> 4

* = Least effective at surface of wheat.

(7) Effect of reduced O_2 (O_2 lack) on susceptibility of certain insects to ethylene oxide as measured by the LC_{100} for 30 minute exposure at 25°C: 608

Insect	Stage	Vacuum Held At (inches)	LC_{100} (mg/l)
Sitophilus oryzae	adult	0 (no vacuum)	48
Sitophilus oryzae	adult	29	24
Ephestia kühniella	larva	0	80
Ephestia kühniella	larva	29	35
Tribolium confusum	pupa	0	141
Tribolium confusum	pupa	29	22

(8) Post-fumigation effects of ethylene oxide—CO_2 mixture on larvae of Lasioderma serricorne larvae exposed in tobacco to ethylene-CO_2 mixture 58.7 lb/1000 ft^3 (4.9 lb/1000 lb tobacco) absolute pressure 0.86 - 1.0 inch, temp. 83°-89°F. To show that gas retained by sorption in tobacco exercises a post-fumigant effect after removal from fumigation chamber and 2 air washings after a 4 hrs exposure to the fumigant: 2592

Treatment, Mortality At Period Of Exposure	Average % Kill At Designated Depth In Baled Tobacco				
	1 1/4 in.	3 1/4 in.	5 1/4 in.	7 1/4 in.	9 1/4 in.
24 hr post fumigation (left in tobacco)	97	83.3	90.2	88.7	84.6
removed at end of 4 hr exposure	88.9	81.2	77.4	82.0	81.5
48 hr post fumigation (left in tobacco)	97	93.4	80.2	83.7	84.2
removed at end of 4 hr exposure	86.3	77.4	55.9	73.9	69.7
72 hr post fumigation (left in tobacco)	100	94.0	92.9	89.0	89.0
removed at end of 4 hr exposure	96.0	94.6	91.0	84.0	81.8

(9) Absorption ratio of ethylene oxide and other fumigants in the presence of flour at 25°C, 760 mm Hg as measured by the LC_{50} in the absence and the presence of flour in the fumigating apparatus: 1013

Fumigant	LC_{50} (mg/l) (Empty Vessel; No Absorbent)	LC_{50} (mg/l) (In Presence Of Flour)	Absorption Ratio	Boiling Point Of Fumigant (°C)
Methyl bromide	10.2	21	2	4.5
Ethylene oxide	15.5	96	6	11
Hydrocyanic acid	—	—	2	26
Methyl formate	18	78	4	32
Carbon disulfide	64	147	2.5	46
Ethyl formate	22	90	4	54
Ethylene dichloride	46	240	5	84
Propylene dichloride	45	235	5	97
Chloropicrin	3.9	35.5	9	112
Tetrachloroethylene	54	440	8	120
Methyl thiocyanate	1.4	14	10	130

(10) Toxicity of ethylene oxide for Aspidiotus perniciosus (San José scale) on nursery stock: 222

Concentration (g/m^3) (C)	Fumigation Time (Hrs) (T)	C × T	% Mortality
15	.2	3	51.9
15	.4	6	63.7
15	.66	10	64.2
15	1	15	72.4
15	1.33	20	80.9
15	1.66	25	99.0
15	2	30	100

4) Pharmacological, pharmacodynamical, physiological, etc.; insects:

a) Considered a general protoplasmic poison. Ethylene oxide brings about the precipitation and denaturation of proteins. The toxic effects are slow to develop; insects after exposure may appear normal but die, nonetheless, in several days. It has been conjectured that ethylene oxide is metabolically converted to formaldehyde or oxalic acid in the insect body. 412 2484

b) Resistance of insects to ethylene oxide:

(1) The existence of a strain ("population") of Aonidiella aurantii which shows marked resistance to ethylene oxide as compared with other strains ("populations") has been reported. 2560

(2) Resistant strains of Saissetia oleae and Coccus pseudomagnoliarum have also been reported. (also see HCN, this work) 2560 2559

5) Miscellaneous observations, remarks:

a) The eggs of Tribolium confusum are killed by $\frac{1}{9}$th of the concentration of ethylene oxide required to kill adults. 612

b) Eggs and adults of Cimex rotundatus, the tropical bed bug, are more readily killed by ethylene oxide than the comparable stages of Cimex lectularius. 1446

c) By using 1 lb/1000 ft^3 in 20 hour exposures, control of common warehouse and household insects may be had. Penetration into cereal packages, furniture is good. 3 lb/1000 ft^3 gave complete kill of Sitophilus oryzae and Tribolium confusum in 3 hours. Addition of 14 lbs CO_2/1000 ft^3 reduced the exposure for 100% kill to 45 minutes. 617

d) Vs. Cimex lectularius (older nymphs) fumigated at 20 mg/l, exposure 5 hours, at 77°F, 760 mm Hg the following mortalities were achieved: Insects wrapped in cotton batting: 37.7% kill; insects wrapped in woolen blanket: 17.8% kill; insects wrapped in woolen blanket inside a barracks bag: 24.2% kill. 2622

Addendum:

1) Recent experiences of the effect on the stability of certain B vitamins exposed to ethylene oxide in the presence of choline chloride have been published by Bakerman, H., et al., Journal of Agricultural and Food

Chemistry 4 (11): 956, 1956.* The following conclusions have been drawn from these recent studies:

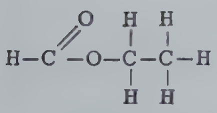
a) Crystalline B vitamins suspended in starch with choline chloride and exposed to ethylene oxide (8.84 g in a 10 l vessel at 24°C for 18 hrs.) showed the following effects:
   (1) Destruction of virtually all the thiamine (and also cocarboxylase added in a concentration equivalent to 100 μg thiamine/g of mixture.)
   (2) Large amounts of the riboflavine, pyridoxine, niacin and folic acid were also destroyed by such treatment.
   (3) Ca. 40% of the thiamine in a stock diet was destroyed by ethylene oxide exposure. The diet concerned was Hunt Club dog meal.
   (4) Pantothenic acid, biotin, vitimin B_{12} in ethylene oxide exposed vitamin mixtures were unharmed.

b) Increase in pH, it is suggested, may account for part of the effect on thiamine of ethylene oxide exposure in presence of choline chloride. This alkalinity cannot explain the destruction of niacin, riboflavine and folic acid—the mechanism of which, under the stated experimental conditions, remains unknown.

*Attention was drawn to this paper too late to permit its inclusion in the alphabetic cumulative bibliography of this work.

90

ETHYL FORMATE



$H-\overset{O}{\overset{\|}{C}}-O-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$

Molecular weight: 74

GENERAL

[Refs.: 353, 2815, 1059, 757, 539]

A low boiling point liquid insecticidal fumigant which has been tested against a rather wide range of stored products, and other, insects, and which may find some practical use under certain conditions.

PHYSICAL, CHEMICAL

A volatile, colorless, flammable liquid; m.p.-80°C; b.p. 54°C; $d_{4°}^{25°}$ 0.924; $n_D^{20°}$ 1.3597; v.p. 255 mm Hg at 25°C; soluble in water to the extent of 0.25 g/100 cc; soluble in many organic solvents; flash point (open cup) - 20°C; decomposes in water to yield ethanol and free acid; miscible with alcohol, ether; to be kept tightly closed and preferably in contact with calcium chloride. 2221

a) Maximum amount in pounds of ethyl formate which may exist as a vapor, at various temperatures, in a 1000 ft³ fumigating chamber: 2671

Temperature (°F)	V.P. (mm Hg)	Lbs As Vapor/1000 ft³
32	64	17
59	164	42
68	207	52
77	255	62
86	312	75
95	382	92
104	462	109
113	558	130
122	668	153

TOXICOLOGICAL

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage	Remarks	
Rat	inh	LC	24.2 mg/l; 8000 ppm	Exposure 4 hours.	2907

2) Phytotoxicity: No data available to this compilation at time of preparation.

3) Toxicity for insects:

a) Quantitative

Insect	Route	Dose	Dosage	Remarks	
Cimex lectularius (egg)	Fumig	LC_{95-100}	< 25 mg/l	Exp 5 hrs at 25°C, 12 l empty flask.	2622
Cimex lectularius (older nymph)	Fumig	LC_{95-100}	30 mg/l	Exp 5 hrs at 25°C, 12 l empty flask.	2622
Cimex lectularius (adult)	Fumig	LC_{95-100}	25-30 mg/l	Exp 5 hrs, at 25°C, 12 l empty flask.	2622
Dacus dorsalis (naked eggs 23-26 hr.)	Fumig	LC_{50}	> 104 mg/l	Exp 2 hrs at 71°-80°F, in empty vessels.	255
Limonius californicus (larva)	Fumig	LC_{50}	16.65 mg/l	Relative toxicity = 1.9 (CS_2 = 1.0).	1957
Limonius californicus (larva)	Fumig	LC_{100}	28.3 mg/l		1957
Stiophilus granarius (adult)	Fumig	LC_{50}	29 mg/l	Exp 5 hrs at 25°C, in empty flasks.	2816, 156
Sitophilus granarius (adult)	Fumig	LC_{50}	35 mg/l	Exp 5 hrs at 25°C, 5-6 l flasks 50 insects/trial.	984
Sitophilus granarius (adult)	Fumig	LC_{99} (calc)	49 mg/l	Exp 5 hrs at 25°C, in empty flasks.	2816, 156
Sitophilus oryzae (adult)	Fumig	LC_{50}	17.5 mg/l	Exp 5 hrs at 25°C, in empty flasks.	2816, 156
Sitophilus oryzae (adult)	Fumig	LC_{99} (calc)	35.5 mg/l	Exp 5 hrs at 25°C, in empty flasks.	2816, 156
Sitophilus oryzae (adult)	Fumig	MLC_{100} 48 hr.	72 mg/l	Exp 24 hrs at ca 25°C, 500 cc flasks with 200 g wheat.	2670
Tribolium confusum (adult)	Fumig	LC_{50}	24.5 mg/l	Exp 5 hrs, at 25°C, in empty flasks.	2816, 156
Tribolium confusum (adult)	Fumig	LC_{99} (calc)	32.5 mg/l	Exp 5 hrs, at 25°C, in empty flasks.	2816, 156

b) Comparative toxicity, ethyl formate and other fumigants:

(1) Consult the various tabulations in the section of this work titled Fumigants, General Treatment.

c) Comparative toxicity, ethyl formate and other alkyl formates:* Refs.: [2816, 156, 2670, 1957, 255, 1958, 984]

Insect		mg/l Formates						
	Dosage	Ethyl	Methyl	Isobutyl	n-Propyl	Isopropyl	Isoamyl	Allyl
Tribolium confusum	LC_{50}	24.5	23.5	—	—	—	—	—
Tribolium confusum	LC_{99}	32.5	37.5	—	—	—	—	—
Limonius californicus	LC_{50}	16.65	12.5	—	—	—	—	102.2**
Limonius californicus	LC_{100}	28.3	23	—	—	—	—	—
Sitophilus oryzae	MLC_{100}***	72	39	35	72	53	70	38
Sitophilus granarius	LC_{50}	35	20; 15	—	28	34	—	—
Sitophilus granarius	LC_{99}	49	36	—	—	—	—	—
Dacus dorsalis (eggs)	LC_{50}	> 104	65	—	—	—	—	—
Dacus dorsalis (eggs)	LC_{95}	—	110	—	—	—	—	—

*Experimental conditions differ rather considerably.

**In presence of soil.

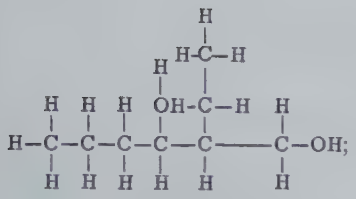
***In presence of wheat grain.

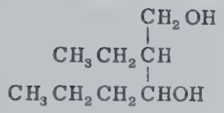
d) Comparative toxicity and absorption ratio, ethyl formate and methyl formate, for *Tribolium confusum*, exposed in empty vessels, and in vessels containing wheat flour; exposed at 25°C, 760 mm Hg: 1013

Fumigant	LC_{50} (Empty Vessel) (mg/l)	LC_{50} (Presence Of Flour) (mg/l)	Absorption Ratio	B. P. (°C)
Ethyl formate	22	90	4	54
Methyl formate	18	78	4	32

91

2-ETHYL-1, 3-HEXANEDIOL (Rutgers 612; 2-Ethyl-3-propyl-1, 3-propanediol; 3-Hydroxymethyl-n-heptan-4-ol; Ethylhexanediol; Ethyl hexyene glycol; Ethohexadiol; 612 Insect Repellent.)





$$\begin{array}{l} \qquad\qquad\quad CH_2OH \\ \qquad\quad\;\; | \\ CH_3CH_2CH \\ \qquad\quad\;\; | \\ CH_3CH_2CH_2CHOH \end{array}$$

Molecular weight: 146.22

GENERAL

[Refs.: 1251, 774, 1804, 3116, 1801]

A compound, repellent to many biting insects, which can be safely applied to the human skin. The mammalian toxicity is quite low and when properly used the irritant properties are at a minimum, as has been extensively demonstrated by wide use among soldiers in the field. 2-Ethyl-1,3-hexanediol emerged as a repellent of promise from an extensive program of screening begun some 20 years ago. In mixture [2-ethyl-1,3-hexanediol (2 parts), dimethyl phthalate (6 parts), Indalone® (2 parts)] the compound formed part of a standard, all-purpose, repellent for military use. This latter formulation is not without drawbacks and is less than ideal. A succinct, general treatment of repellents and repellency may be found in Ref. 774.

At present, 2-ethyl-1,3-hexanediol finds use in a new military repellent formulation (M-2020) made up of dimethyl phthalate 40%, 2-ethyl-1,3-hexanediol 30%, and dimethyl carbate 30%. Applied to the skin, M-2020 is effective in repelling anopheline mosquitoes for ca. 2 hours, Aëdes spp., ticks, chiggers for ca. 4 hours.

PHYSICAL, CHEMICAL

A colorless, somewhat oily liquid; freezing point below -40°C; b.p. 244.2°C; distillation range for the crude product 240-250°C; d$^{20°}_{20°}$ (pure) 0.9422, d$^{20°}_{20°}$ (crude) 0.939; d$^{20°}_{20°}$ (crude) 0.943; n$^{20°}_{D}$ 1.451; v.p. <0.01 mm Hg at 20°C ; viscosity = 323 centipoises at 20°C; flash point 260°F; bulk density at 20°C=7.84 lb/gallon; soluble in water to 4.2% at 20°C; soluble in ethanol, isopropanol, propylene glycol, castor oil; odor (crude product): Witch hazel-like; stable under ordinary conditions; no effect on clothing or most plastics; will not dissolve rayon or nylon.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage	Remarks	
Mouse	or	LD_{50}	1.9 cc/k		842
Rat	or	LD_{50}	1.4 cc/k		842
Guinea Pig	or	LD_{50}	4.2 cc/k		842
Chicken	or	LD_{50}	2.5 cc/k		842
Rabbit	or	LD_{50}	2.6 cc/k		841
Rabbit	ct	LD_{50}	2 cc/k/day	For 90 days.	841

2) Effect on insects, other arthropods:
- a) Under the conditions of certain screening tests the following results are reported: 1801
  - (1) Insecticidal, ovicidal, "knockdown" properties for Pediculus humanus corporis, Anopheles quadrimaculatus (4th instar larva), Trombicula splendens, Eutrombicula alfreddugesi:
    - (a) Lice on impregnated cloth: 100% kill on initial exposure; ineffective on a second exposure 1 day after treatment.
    - (b) Louse eggs, by dipping: 2-ethyl-1,3-hexanediol fell in a class giving 51-99% kill in 5% solution.
    - (c) Louse "knockdown": Complete "knockdown" in 24, but not in 3 hours.
    - (d) As a mosquito larvicide: In a class of compounds giving less than 50% kill in 48 hours at 10 ppm.
    - (e) Chiggers, insecticidal and "knockdown" action: Effective toxicant action on initial test of impregnated cloth patches, but ineffective after one 15 minute rinse; "knockdown": 100% in 1-5 minutes.
  - (2) Repellency:
    - (a) For mosquitoes: On skin, Aëdes aegypti, repellent for 300 or more minutes; Anopheles quadrimaculatus, repellent for 31-60 minutes; Aëdes taeniorhynchus, A. sollicitans repellent for 180 minutes.

On clothing: Effective for more than 21 days for Aëdes aegypti, 6-10 days for A. taeniorhynchus, A. sollicitans, 1-5 days for Anopheles quadrimaculatus. In clothing wearing tests: Repellency for Aëdes aegypti, Anopheles quadrimaculatus retained through 16-24 hours of wearing; for A. taeniorhynchus, A. sollicitans for 0-8 hours wearing. In washing tests: 2-Ethyl-1,3-hexanediol on clothing proved ineffective in repelling Aëdes aegypti after one rinse.

(b) For fleas, ticks: Ineffective in repelling Xenopsylla cheopis, Ctenocephalides felis (cloth patch tests) after one day; effective for 1-5 days in repelling Amblyomma americanum (cloth patch tests).

3) Comparative repellency evaluations of 2-ethyl-1,3-hexanediol and other compounds: 1804

a) Usual treatment = 2 g repellent/ft^2 of cloth (ca 5% of dry weight).

(1) Vs. mosquitoes: Aëdes aegypti = I, Aëdes taeniorhynchus = II, Anopheles quadrimaculatus = III:

2-Ethyl-1,3-hexanediol vs. I, III withstands 27 days aging, 16 hours wear.
Methyl-N,N'-diisopropyl adipamate vs. I, II, III effective to 149 days aging 56 hrs. wear.
2-Butyl-2-ethyl-1,3-propanediol vs. I, II, III effective to 149 days aging, 56 hrs. wear.
N-Butyl-1,2,3,6-tetrahydrophthalamide effective at least 10 days after clothing treatment and through several days wear. The same is true of Indalone®, undecylenic acid, α-butoxy-N-cyclohexylacetamide.
2,4-Nonanediol vs. III effective at least 10 days after treatment and for several days wear.
Dimethyl phthalate vs. III withstands 27 days aging, 16 hours of wear.

(2) The following are effective in repelling Amblyomma americanum after at least 10 days aging and through several days of wear:

N-butylacetanilide, hexyl mandelate, Indalone®, α-butoxy-N-cyclohexylacetamide.
N,N-dibutylacetoacetamide, N-propylacetamide, undecylenic acid.

(3) The following are effective repellents for fleas, Xenopsylla cheopis, Ctenocephalides felis, for at least 10 days of aging and through several days wear:

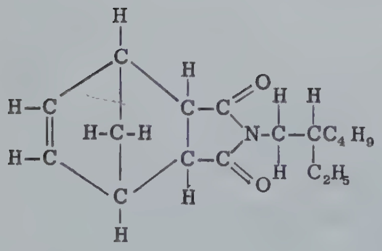
Undecylenic acid, benzyl benzoate, N-butylacetanilide, N-propylacetanilide, hexyl mandelate.

(4) The following remain effective repellents for Trombicula masoni, T. alfreddugesi after 6 or more launderings of treated clothing:

Diphenyl carbonate, benzil, p-tolyl benzoate. Effective after 3-4 launderings are: benzyl benzoate, dibutyl phthalate, dimethyl phthalate.

92

N-(2-ETHYLHEXYL)-BICYCLO-[2. 2. 1]-5-HEPTENE-2, 3-DICARBOXIMIDE (MGK 264®; Van Dyk 264; Octacide 264; N-Octyl bicycloheptene dicarboximide; N-2-Ethylhexylimide of endomethylene tetrahydrophthalic acid.)



Molecular weight: 275.378

GENERAL

[Refs.: 2366, 1423, 2292, 2291, 2231, 2120]

The insecticidal properties of this compound were described first in 1949. The action is primarily one of synergism with the pyrethrins, and particularly allethrin, q.v., whose activity in fly sprays for Musca domestica it greatly enhances so that the mortality yielded by a given quantity of pyrethrins or allethrin alone is greatly increased when this same amount is combined with an appropriate proportion of MGK 264®. Consult, in this work, the general treatment titled Synergism, Synergists.

PHYSICAL, CHEMICAL

[1423, 310, 309, 2161]

The technical product (ca 99%pure): A viscous liquid; b.p. 158°C at 2 mm Hg; $d^{18°}_{18°}$ 1.05; $n^{20°}_{D}$ 1.505; insoluble in water; miscible with Freon®, petroleum oils and most organic solvents; a solvent for DDT, BHC, lindane; related to N-butyl- and N-amyl-imides, which also show synergistic action with pyrethrins; prepared by heating the condensation product of cyclopentadiene and maleic anhydride with an equimolar amount of 2-ethylhexylamine, in the presence of a solvent, until the required amount of water has been eliminated.

TOXICOLOGICAL

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}(ca)	2800		1951
Rabbit	ct	LD_{50}(ca)	470	Applied as a 5% suspension in water.	1952

a) Has been incorporated in the diet of rats at 5000 ppm over a period of 17 weeks without evidence of damage. 1953

2) Toxicity for insects:

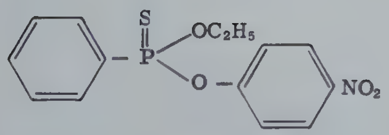
a) Effects of MGK 264® on the toxicity of allethrin toward *Blattella germanica* treated by a direct spray method, and a comparison of the action with two related synergizing substances: 2291

Compound	Concentration (g/100 cc)	% Mortality In 72 Hrs At 0.5 cc Dosage	% Mortality In 72 Hrs At 1.0 cc Dosage
Allethrin (alone)	0.1	2.5	11.2
Pyrethrins (alone)	0.1	23.8	96.2
Allethrin + MGK 264®	1.0	12.5	82.5
Allethrin + MGK 264®	2.0	55.0	99.0
Allethrin + 2-Ethylbutylimide of endomethylene tetrahydrophthalic acid	2.0	51.2	100
Allethrin + 1-Methylisobutylimide of endomethylene tetrahydrophthalic acid	2.0	21.2	96.5

93

ETHYL-p-NITROPHENYL BENZENETHIONOPHOSPHONATE

(EPN®; Ethyl-p-nitrophenyl thionobenzene-phosphonate; O-Ethyl-O-p-nitrophenyl phenylphosphonothioate; Ethyl-p-nitrophenyl thiobenzene phosphonate.)



Molecular weight: 303.301

GENERAL

[Refs.: 874, 2120, 129, 353, 1553, 2076, 713]

An insecticide and acaricide belonging to the general class of compounds referred to as organic phosphate or "organophosphorus" insecticides. (See, in this work, the section titled Organic Phosphates for data and considerations pertinent to these insecticides as a group.) EPN® has shown a wide "spectrum" of activity against insects and mites. EPN® is highly toxic to warm blooded animals. Phytotoxic hazard is apparently of a very low order, under proper application. EPN® acts upon susceptible insects and acarines by contact and as a stomach poison; it possesses little, if any, fumigant action. EPN® is described by the manufacturer as a highly hazardous chemical, to be handled as such. Toxicity for man may be manifested via ingestion, inhalation, skin absorption, and all precautions of protective clothing, gloves, goggles, respirators, etc., are rigourously recommended.

PHYSICAL, CHEMICAL

[Refs.: 874, 2248, 2120, 129, 2231]

Pure: A white crystalline solid; technical: A dark amber liquid; m.p. (pure) 36°C; $d_{4°}^{25°}$ (technical) 1.268; $n_D^{30°}$ (technical) 1.5978; v.p. 3×10^{-4} mm Hg at 100°C (0.03 mm Hg); virtually insoluble in water; soluble in most of the common organic solvents; stable at ordinary temperatures and in neutral and acid media; undergoes slow

hydrolysis in alkaline media to free p-nitrophenol, the first order rate constant at 37°C being: $K = 13.8\ OH^-\ min^{-1}$. EPN® is compatible with most of the usual insecticides and fungicides, except for those whose water solutions are highly alkaline, for example, lime, lime-sulfur, Bordeaux mixture, basic lead, zinc and calcium arsenates.
Formulations: Principally as a wettable powder, in commerce; as emulsifiable concentrates available for special uses only from the manufacturer; dust mixtures are available in some places, but the manufacturer does not recommend the formulation of EPN® 300 Insecticide (the wettable powder) as a dust, and users are urged not to dilute EPN 300 as a dust because of the hazard involved.

TOXICOLOGICAL

1) General: EPN® is described as moderately toxic to some species, highly toxic to others. Marked differences in susceptibility of the sexes is remarked in some species. Freshly purified crystalline EPN® has no anti-choline esterase activity in vitro; however, the acute toxicity of crystalline EPN®, orally, for the Guinea pig is equal to the toxicity of impure samples, which are active against choline esterase in vitro. 1553
   a) Toxicity, compared to DDT = 1: Acute oral 17; chronic oral 0.33; dermal single dose 200. Ca. $\frac{1}{5}$th as toxic as parathion. 2345 1950

2) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse ♂,♀	or	LD$_{50}$	45.5 ± 3.1		1057
Mouse ♂	ip	LD$_{0}$ 24 hr	34	Technical EPN®.	874
Mouse ♀	ip	LD$_{0}$ 24 hr	27	" .	874
Mouse ♂	ip	LD$_{100}$24 hr	69	" .	874
Mouse ♀	ip	LD$_{50}$ 24 hr	48 ± 13	" .	874
Mouse ♀	ip	LD$_{100}$24 hr	87	" .	874
Mouse ♂	ip	LD$_{0}$ 24 hr	140	EPN® 300, wettable powder.	874
Mouse ♂	ip	LD$_{50}$ 24 hr	410 ± 120	" " .	874
Mouse ♀	ip	LD$_{0}$ 24 hr	76	" " .	874
Mouse ♀	ip	LD$_{50}$ 24 hr	380 ± 60	" "	874
Mouse ♂	ip	LR*	34-69	*Lethal Range; EPN® technical.	1553
Mouse ♀	ip	LD$_{50}$	48	Technical EPN®; in peanut oil.	1553
Rat ♂	or	LD$_{0}$ 24 hr	11	" .	874
Rat ♀	or	LD$_{0}$ 24 hr	5	" .	874
Rat ♂	or	LD$_{0}$ 24 hr	52	EPN® 300, wettable powder.	874
Rat ♀	or	LD$_{0}$ 24 hr	10	" " .	874
Rat ♂	or	LD$_{50}$ 24 hr	40 ± 5	Technical EPN®.	874
Rat ♀	or	LD$_{50}$ 24 hr	12 ± 3	"	874
Rat ♂	or	LD$_{50}$ 24 hr	76 ± 4	EPN® 300, wettable powder.	874
Rat ♀	or	LD$_{50}$ 24 hr	19 ± 2	" "	874
Rat ♂	or	LD$_{50}$	42	Crystalline EPN®, in peanut oil.	1553
Rat ♀	or	LD$_{50}$	14	" " .	1553
Rat ♂	or	LD$_{50}$	91.4 ± 8.6		1057
Rat ♀	or	LD$_{50}$	14.5 ± 1.6		1057
Rat ♀	or	LD$_{50}$	7; 8; 13	Technical EPN®, in peanut oil; 4 lofs subjects.	1553
Rat ♂	or	LD$_{50}$	28; 33	Technical EPN®, in peanut oil; 2 lofs subjects.	1553
Rat ♂	or	LD$_{100}$24 hr	70	Technical EPN®.	874
Rat ♀	or	LD$_{100}$24 hr	26	"	874
Rat ♂	or	LD$_{100}$24 hr	126	EPN®300, wettable powder.	874
Rat ♀	or	LD$_{100}$24 hr	41	" "	874
Rat ♂	ip	LD$_{0}$ 24 hr	33	Technical EPN®.	874
Rat ♀	ip	LD$_{0}$ 24 hr	19	"	874
Rat ♂	ip	LD$_{0}$ 24 hr	130	EPN®300, wettable powder.	874
Rat ♀	ip	LD$_{0}$ 24 hr	20	" "	874
Rat ♂	ip	LD$_{50}$ 24 hr	108 ± 32	Technical EPN®.	874
Rat ♀	ip	LD$_{50}$ 24 hr	26 ± 2	"	874
Rat ♂	ip	LD$_{50}$ 24 hr	74 ± 1	EPN®300, wettable powder.	874
Rat ♂	ip	LD$_{50}$	64	Technical EPN®, in peanut oil.	1553
Rat ♀	ip	LD$_{50}$	24	" "	1553
Rat ♂	ip	LD$_{100}$24 hr	204	Technical EPN®.	874
Rat ♀	ip	LD$_{100}$24 hr	52	"	874
Rat ♂	ip	LD$_{100}$24 hr	200	EPN®300, wettable powder.	874
Rat ♀	ip	LD$_{100}$24 hr	462	" "	874
Guinea Pig ♂,♀	or	LD$_{50}$	79.4 ± 7.6		1057
Guinea Pig ♂	ip	LD$_{0}$ 24 hr	10	Technical EPN®.	874
Guinea Pig ♀	ip	LD$_{0}$ 24 hr	20	"	874
Guinea Pig ♂	ip	LD$_{0}$ 24 hr	18	EPN®300, wettable powder.	874
Guinea Pig ♀	ip	LD$_{0}$ 24 hr	18	" "	874
Guinea Pig ♂	ip	LR	10-20	EPN®Technical, in peanut oil.	1553

2) Acute toxicity for higher animals: (continued)

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Guinea Pig ♀	ip	LR	20-30	EPN® Technical, in peanut oil.	1553
Guinea Pig ♂	ip	LD$_{100}$24 hr	20	Technical EPN®.	874
Guinea Pig ♀	ip	LD$_{100}$24 hr	30	"	874
Guinea Pig ♂,♀	ip	LD$_{100}$24 hr	35	EPN® 300, wettable powder.	874
Rabbit ♂	ct	LD$_0$ 24 hr	30	Technical EPN®.	874
Rabbit ♀	ct	LD$_0$ 24 hr	90	"	874
Rabbit ♂	ct	LD$_0$ 24 hr	1050	EPN® 300, wettable powder.	874
Rabbit ♀	ct	LD$_0$ 24 hr	1050	" "	874
Rabbit ♂	ct	LR	30-50	Technical EPN®.	1553
Rabbit ♀	ct	LR	90-150	"	1553
Rabbit ♂	ct	LD$_{100}$24 hr	50	"	874
Rabbit ♀	ct	LD$_{100}$24 hr	150	"	874
Rabbit	ct	LD$_{50}$	ca2000	EPN® 300, wettable powder, (quoting Frawley.)	874
Rabbit ♂	ip	LD$_0$ 24 hr	40	Technical EPN®.	874
Rabbit ♀	ip	LD$_0$ 24 hr	10	"	874
Rabbit ♂	ip	LD$_0$ 24 hr	18	EPN® 300, wettable powder.	874
Rabbit ♀	ip	LD$_0$ 24 hr	35	" "	874
Rabbit ♂	ip	LD$_{100}$24 hr	80	Technical EPN®.	874
Rabbit ♀	ip	LD$_{100}$24 hr	20	"	874
Rabbit ♂	ip	LD$_{100}$24 hr	35	EPN® 300, wettable powder.	874
Rabbit ♀	ip	LD$_{100}$24 hr	52	" "	874
Rabbit ♂	ip	LR	40-80	Technical EPN®, in peanut oil.	1553
Rabbit ♀	ip	LR	10-20	" "	1553
Dog ♂	or	LR	20-30	Crystalline EPN®, in peanut pil.	1553
Dog ♀	or	LR	20-45	" "	1553
Dog ♂	or	LR	2-50	Technical EPN®, in peanut oil.	1553
Dog ♀	or	LR	2-75	" "	1553
Dog ♂	ip	LD$_0$ 24 hr	9	Technical EPN®.	874
Dog ♀	ip	LD$_0$ 24 hr	17	"	874
Dog ♂	ip	LD$_{100}$24 hr	13	"	874
Dog ♀	ip	LD$_{100}$24 hr	25	"	874
Dog ♂	ip	LR	9-35	Technical EPN®, in peanut oil.	1553
Dog ♀	ip	LR	17-50	" "	1553

3) Chronic toxicity and sub-acute toxicity; higher animals:

a) 30 day feeding tests; rats: 1553,1953

Sex	Ppm In Diet	Effects On		Deaths	Symptoms
		Growth	Organ Weights		
♂	100	0	0	—	
♂	300	+ ↓	0	—	
♂	600	+ ↓	0	some	Excitability, tremors reaching peak in 2nd week; disappeared end of 4th wk.
♀	35	0	0	—	
♀	100	+ ↓	0	—	
♀	300	+ ↓	0	some	Excitability, tremors; peak in 2nd wk, disappeared end of 4th wk.

b) 2 year feeding tests; rats: + = effect, 0 = no effect or none, to suit context. 1553

Sex	Ppm	Effects On					Pathology Major Organs	Estimated Daily EPN Intake (mg/k)	Symptoms
		Growth	Mortality	Blood, Urine	Organ Wgts	EPN® Storage			
♂	50	0	0	Normal	0	0	0	3	0
♂	150	0	0	Normal	0	0	0	10	0
♂	450	+ ↓	0	Normal	0	0	0	29	As in 30 day tests.
♀	25	0	0	Normal	0	0	0	1	0
♀	75	0	0	Normal	0	0	0	4	0
♀	225	+ ↓	0	Normal	0	0	0	12	As in 30 day tests.

c) 1 year feeding tests; dogs: 1553

(1) Preliminary tests: 4 mg/k daily were tolerated by one animal without toxic response for 3 weeks; for 8 weeks (ca.) by another subject. 8 mg/k/day were not tolerated. No evidence of specific histopathological changes.

	Effects On					Histopathology	Choline esterase**
			Wgt Of				
mg/k/day	Blood	Urine	Organs*	Kidneys	CNS	Major Organs	
0.1	0	0	0	↑ Wgt with increasing dosage	0	0	Early ↓ correlated with dosage; by end of year, levels entirely comparable to controls.
0.5	0	0	0		0	0	
2.0	0	0	0		0	0	

*Liver, lungs, heart, brain, spleen. **Tests at 3 mg/k/day gave rapid decline in ChE levels; subjects failed rapidly. 874

4) Effects of EPN® on mammalian choline esterase (ChE): 1553

a) Water extracts of EPN® crystalline (not highly purified) gave marked inhibition of human erythrocyte ChE, slowly increasing with time; under conditions of experiments cited, decrease of ChE activity to 53% of initial activity occurred in 200-300 minutes.

b) EPN® ChE inhibition is irreversible. Reaction between ChE and EPN is a reaction of the second order.

c) EPN®, recrystallized, freshly purified, lacks ChE inhibitory activity in vitro; the oral, acute, toxicity (Guinea Pigs) is the same for samples of the highest purity and of lesser purity.

(1) Postulated that rapid conversion of highly purified EPN® to a substance of active anti-ChE activity occurs in vivo; anti-ChE activity develops spontaneously in water + highly purified EPN® on standing, the active contaminant being effective at concentrations $> 10^{-8}$ M; no evidence exists to link this spontaneously developing contaminant with the in vivo lethal agent; molecular nature of the in vitro ChE inhibitor is unknown.

5) Pharmacological, pharmacodynamical, physiological, etc.:

a) The foregoing data on chronic and subacute toxicity hints the mechanism of toxicity in the case of EPN®. 1553
The intoxication is cholinergic, with the appropriate CNS manifestations, the virtual absence of histopath- 1458
ology and the progressive decline of cholinesterase activity of blood and tissues. The active principle of 2231
toxicity in poisoned animals is apparently a substane derived (metabolically?) from the toxicant as introduced. Consult, in this work, the section titled Organic Phosphates.

(1) Atropine is indicated as the antidote for the "muscarinic" effects of EPN®. 874

(2) For EPN® intoxicated rats, coramine + atropine therapy is reported superior to the application of either drug alone; analeptics, such as metrazol, amphetamine, picrotoxin, caffeine, enhance the mortality of EPN® intoxicated subjects. 1458

6) Residues; residue hazards: 874,1298

a) Dosage level and frequency of application influence initial residue levels. 874

(1) Degradation of EPN® on plant surfaces is so rapid that high dosage rates, frequent early season treatments, do not, at harvest, increase the residue levels proportionately.

(2) Highest residues ($>$ 8 ppm) occurred on peaches (fuzzy-skinned fruit). 874, 129

b) 192 analytical results (reporting on 14 crops) showed 96% to fall below 8 ppm. On basis of values taken 15 days or more after last EPN® application, 99% of reported residue values fell below 8 ppm.

c) Not to be used as a dust or during the blossoming of fruit trees or later than July 15th on olives or later than the following number of days prior to picking or harvesting: Citrus 30 days, corn 14 days, others 21 days. 874

d) Initial residues of 75 $\mu g/cm^2$ on apple foliage declined in 14 days to 3 $\mu g/cm^2$ with half-life of 3 days; On peach fruits initial residue of 9.5 ppm declined to 3.4 in 14 days with half-life of 10 days; On peach foliage initial residues of 10.5 $\mu g/cm^2$ declined to 2.1 $\mu g/cm^2$ in 14 days with half-life of 6 days. 1298

e) Comparative half-life values in days for EPN®, other acaricides in citrus peel: 1302

Acaricide	Half-life In Days
EPN®	ca. 80
Aramite®	7-8
Ovotran®	10
DDT	30-40
Dieldrin	8-10
Parathion	60-80
Sulphenone	9-12
Chlorobenzilate®	60-80

7) Phytotoxicity:

a) The general phytotoxic hazard appears to be very low. 874, 129

(1) Injury has been noted on young tender growth of apple trees of the Fameuse-McIntosh cultivar groups. 2120, 353

(2) Damage reported to cucumbers (Cucurbitaceae); "burning" of "Marketer" cultivar sprayed with EPN®,300 at 1 lb/100 gallons and dusted with 1% EPN® dust. 874, 129

8) Toxicity for insects; acarines:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aëdes nigromaculis (4th instar)	Medium	LC_{50} 24 hr	0.000862 ppm		1193
Anasa tristis (adult)	Topical	LD 72 hr	128 µg/g	In acetone sol.; 100% mortality.	3376
Anopheles quadrimaculatus (larva)	Medium	MLC_{100}	0.005 ppm		2020
Apis mellifera (larva)	Topical	LD_{50}	3.0 µg/g		2231
Chrysops discalis (adult)	Topical	LD_{50} (estimate)	48 µg/fly		2707
Chrysops discalis (adult)	Topical	LD_{90}	120 µg/fly		2707
Conotrachelus nenuphar (adult)	Topical	LC_{50}	32 ppm	At 80°F; by dipping in H_2O susp; ca 1/2 as toxic as parathion.	2864
Conotrachelus nenuphar (adult)	Residual	MED*	68 mg/100 cm^2	*=Minimum effective residue; ca 1/2 as effective as parathion.	2864
Culex tarsalis (4th instar)	Medium	LC_{50} 24 hr	0.000649 ppm		1193
Musca domestica (adult)	Topical	LD_{50}	1.9 µg/g		2231
Musca domestica (adult)	Topical	LD_{50}	2.0 µg/g		2247
Tetranychus bimaculatus (adult)	Contact Residue	LC_{50}	2.5 mg/100 cc	Emulsifiable concentrate; on plants treated in dusting tower.	905
Tetranychus bimaculatus (adult)	Contact Residue	LC_{50}	4.8 mg/100 cc	Wettable powder; on plants previously sprayed in settling tower.	905
Tetranychus bimaculatus (larva)	Contact residue	LC_{50}	4.7 mg/100 cc	Emulsifiable conc.; on plants previously sprayed in settling tower.	905
Tetranychus bimaculatus (larva)	Contact residue	LC_{50}	7.7 mg/100 cc	Wettable powder; on plants previously sprayed in settling tower.	905
Tetranychus bimaculatus (egg)	Contact residue	LC_{50}	230 mg/100 cc	Emulsifiable conc.; on plants previously sprayed in settling tower.	905
Tetranychus bimaculatus (egg)	Contact residue	LC_{50}	460 mg/100 cc	Wettable powder; on plants previously sprayed in settling tower.	905
Tetranychus bimaculatus (adult)		LC_{50}	42 mg/100 cc	Emuls. conc.; mites on leaf side opposite treated side.	905
Tetranychus bimaculatus (adult)		LC_{50}	76 mg/100 cc	Wett. pwdr.; mites on leaf side opposite treated side.	905
Tetranychus bimaculatus (red form)	Topical	LC_{50} 24 hr	5.5 ppm	By dipping; mites on bean leaves. } difference statistically	565
Tetranychus bimaculatus (green form)	Topical	LC_{50} 24 hr	3.9 ppm	By dipping; mites on bean leaves. } significant.	565
Tetranychus bimaculatus (red form)	Topical	LC_{90} 24 hr	20 ppm	By dipping; mites on bean leaves. } difference statistically	565
Tetranychus bimaculatus (green form)	Topical	LC_{90} 24 hr	12 ppm	By dipping; mites on bean leaves. } significant.	565

b) EPN® vs. Tetranychus bimaculatus, greenhouse tests on Phaseolus coccineus sprayed with 31.5% wettable powder at 0.25 lb/100 gallons; > 700 to > 1500 mites examined per trial: 117

Days Between Spraying And Infesting	% Mortality After 7 days	% Mortality After 14 days	Days Between Spraying And Infesting	% Mortality After 7 days	% Mortality After 14 days
1	98.6	100	10	88.2	100
2	99.4	100	12	93.5	98.9
3	96.4	100	14	86.6	80.0
4	93.0	100	16	90.2	68.8
5	96.1	99.8	18	76.3	66.6
6	87.5	100	20	76.4	70.0
7	90.9	99.7	CONTROL	6.2	4.3

(1) Destruction of introduced mites is rapid. Mature ♀♀ have chance to lay but few eggs before death. Eggs which are laid hatch, but, until 12 days after spraying, new-hatched mites are destroyed. Survival of some new-hatched mites commences after 14 days post-treatment.

c) Comparative toxicity, EPN® and other compounds vs. insects and acarines:

(1) Vs. Conotrachelus nenuphar (adult), topical application by 5 second wetting in water suspensions, at 80° F; insecticides as wettable powders: 2864

Insecticide	LC_{50} (ppm)	Ratio To Parathion	Field Concentration Used (ppm) Giving Control	Initial Deposit µg/100 cm^2
EPN®	32	2.3 : 1	390	455
Parathion	14	1 (standard)	360	349
Dieldrin	104	7.4 : 1	300	270
Methoxychlor	4000	285.7 : 1	1800	2712

	Approx Minimum Effective Residue µg/100 cm^2	
EPN®	68	2 : 1
Parathion	34	1 (standard)
Dieldrin	71	2.1 : 1
Methoxychlor	865	25.4 : 1

Field Experiences: EPN® and other compounds vs. Conotrachelus nenuphar on prune trees:

Year	Application Dates	Control (larvae/tree)	% Control By EPN®	% Control By Parathion	% Control By Dieldrin	% Control By Methoxychlor
1949	5/16 5/26 6/5	1292	—	97.5	—	98.8
1950	6/5 6/15 6/26	790	—	97.2	—	—
1951	5/28 6/8 6/18	1493	99.1	99.3	—	93.1
1952	5/29 6/9	1381	—	90.2	98.9	—
1953	5/25 6/2	384	82.8	66.5	99.2	78.9
1954	5/26 6/4	499	—	89.1	—	—

(a) Break in residual effectiveness occurred in all cases between 4-7 days, being sharpest for parathion, least pronounced for dieldrin, intermediate for EPN® and Methoxychlor.

(b) Direct contact (topical) toxicity not a reliable index to effectiveness of chlorinated hydrocarbons. For EPN® and parathion a rather close relationship is noted between topical and residual toxicity.

(c) EPN® showed residual effectiveness of the order of dieldrin, with quick action and high effectiveness residually and by contact, in cage test determinations. Ovicidal action present and slightly superior to dieldrin. Larvicidal action slightly inferior to dieldrin.

(2) Toxicity EPN® and other compounds vs. DDT-R strains of mosquitoes; Aëdes nigromaculis, Culex tarsalis (4th instar). (Chlorinated hydrocarbons at 10-15 times the normal dosages, applied as larvicides have failed to control the mosquitoes in question in the San Joaquin valley of California:) 1193

Insecticide	LC_{50} 24 Hrs. (ppm) For	
	Aëdes nigromaculis	Culex tarsalis
EPN®	0.000862	0.000649
Tetra-n-propyl dithionopyrophosphate ("TPD")	.0625	.0178
Malathion	.025	.0185
DDT	.0588	.111

(3) Effect of temperature on toxicity of EPN® and other compounds for Culex tarsalis (4th instar): 1193

Insecticide	Ppm	% Mortality (24 Hrs) At	
		70°F	90°F
EPN®	0.00067	57	91
EPN®	.0005	46	79
EPN®	.00025	16	48
EPN®	.0000125	4	24
"TPD"	.033	44	100
"TPD"	.025	17	100
"TPD"	.0167	15	85
Malathion	.033	24	85
Malathion	.025	19	75
Malathion	.0167	8	40

(4) Field tests; effectiveness of EPN® vs. mosquito larvae: 1193

Insecticide And Spraying Method	Lbs Active Ingredient Per Acre	% Mortality 24 Hrs For	
		Aëdes nigromaculis	Culex tarsalis
EPN emulsion (By airplane)	0.045	98	96
	.035	89	89
	.025	45	57
EPN emulsion (By "Jeep")	.035	99	100
	.025	95	98
	.01	89	97
	.005	—	57
EPN suspension (By "Jeep")	.035	99	100
	.025	98	100
	.01	55	97
	.005	—	70
Malathion emulsion (By "Jeep")	.4	99	—
	.3	92	83
	.2	83	97
	.1	—	67
"TPD" emulsion (By "Jeep")	.4	93	—
	.3	89	99
	.2	87	77
	.1	—	76

(5) Comparative toxicity EPN® and other thionophosphate esters for Musca domestica (adult): 2247

Compound	Topical LD_{50} 24 Hrs (µg/g)
EPN®	2.0
Methyl parathion	1.3
Parathion	1.4
Isopropyl parathion	4.8
Malathion	27.0

(6) Toxicity EPN® and other insecticides for Anasa tristis; topical application in acetone solution: 3376

Insecticide	% Mortality 72 Hrs At					Speed Of Action At Lowest Topical Dosage Giving 90% Or > Mortality				
							% Mortality In			
	(µg/g) 32	64	128	256	512	µg/g	12 hrs	24 hrs	48 hrs	72 hrs
Parathion	100	100	100	100	100	6	3.3	33.3	76.7	90
Lindane	83.3	100	100	100	100	64	—	80	100	100
Aldrin		93.3	100	100	100	64	—	23.3	76.7	93.3

(6) Toxicity EPN® and other insecticides for Anasa tristis; topical application in acetone solution: (cont.) 3376

Insecticide	% Mortality 72 Hrs at (µg/g) 32	64	128	256	512	Speed Of Action At Lowest Topical Dosage Giving 90% Or > Mortality µg/g	% Mortality In 12 hrs	24 hrs	48 hrs	72 hrs
Endrin			100	100	100	128	6.7	20	86.7	100
EPN®			100	100	100	128	10	26.7	76.7	100
Heptachlor		83.3	90	100	100	128	10	50	80	90
Isodrin			90	100	100	128	0	10	63.3	90
Dieldrin			70	100	100	256	0	70	96.7	100
Chlordane			36.7	80	90	512	—	6.7	73.3	90
Toxaphene			16.7	66.7	82	—	—	—	—	—
DDT			20	30	76.7	—	—	—	—	—

(7) Toxicity; EPN® and other compounds for adult Chrysops discalis, topical application: 2707

Insecticide	LD_{50} (estimate) (µg/fly)	LD_{90} (µg/fly)
EPN®	48	120
Lindane	4	35
Endrin	9	80
DDT	20	250
Dieldrin	20	950
Methoxychlor	30	90
Aldrin	40	170
Heptachlor	40	200
Isodrin	60	170
Chlordane	60	650
Chlorothion®	65	420
Diazinon	90	360
3-Chloro-4-methyl umbelliferone, O,O-diethyl thiophosphate	90	910
Q-137	120	400
Malathion	130	330
Toxaphene®	180	480

(8) Speed of toxic action, EPN® and other compounds vs. Macrosiphum pisi on bean plants; as dusts (in talc) applied by dusting tower method: 520

Material	Dust Concentration (%)	Temperature (°F)	Time For 50% Kill Hrs	Minutes	98% Kill Hrs	Minutes
Talc	100	67-72	13	28	23	51
Toxaphene®	5	72	13	20	19	1
Chlordane	5	72	9	24	18	8
EPN®	0.86	74	5	26	8	6
Dieldrin	1	75	4	7	6	43
Aldrin	1	75	3	44	7	32
TDE	5	72	2	34	4	35
Methoxychlor	10	75	2	1	5	34
Parathion	1	70	1	8	1	43
Parathion	2	70	1	21	1	53
DDT	5	72	0	57	1	45
Lindane	1	72	0	56	1	54
Rotenone (5% rotenone)	5	72	0	47	1	23
TEPP	.18	74	0	20	0	56
Nicotine	1	72	0	15	1	12
Nicotine	3	72	0	12	0	50

(9) EPN® and other compounds in control of Pyrausta nubilalis* in sweet corn ears; as sprays: 675

Insecticide	Lbs/100 gal.	% Reduction P. nubilalis By Direct Action	By Residual Action
EPN®	0.75	57	79
Heptachlor	1.0	70	77
Aldrin	0.75	70	74
DFDT	1.0	64	73
Dieldrin	0.5	78	49
DDT	1.0	54	40
Parathion	0.5	65	18

*For later data consult Ref. 622.

(10) EPN® and other insecticides as spot treatments vs. Haematopinus eurysternus on cattle; used as emulsion concentrates, wettable powders: 2862

Insecticide	Conc (%)	% Kill 24,48 hrs	Weeks Effective
EPN®	.05	100	1
	.01	100	1
	.005	100	1
	.002	25	0
Parathion	.05	100	3
	.01	100	3
	.005	25	0
Chlorothion®	.25	100	1
Pyrazinon	.25	100	3
Tetrapropyl dithiopyrophosphate	.05	100	1
Bayer 21/199	.25	100	2
	.2	100	2
	.1	100	1
	.05	100	1
2-Pivalyl indanedione	1.0	100	3
	.5	100	2
	.25	100	2
	.1	100	2
	.05	100	2
DDT	.5	100	4
	.25	100	3
Toxaphene®	.5	100	4
Strobane	.5	100	4

Insecticide	Conc(%)	% Kill 24,48 Hr	Weeks Effective
Dipterex®	.25	100	1
	.1	100	0
Malathion	.5	100	2
	.05	100	1
Diazinon	.25	100	2
	.1	100	2
	.05	100	1
	.01	95	1
	.005	25	1
	.002	5	1

(11) EPN® and other substances as dips for goats vs. Bovicola caprae, B. limbatus: 2862

Insecticide	Conc (%)	% Kill 24, 48 Hrs.	Infestation After 4 Weeks
EPN®	.002	100	0
DDT	.25	100	0
Strobane	.2	100	0
	.1	100	0
Endrin	.05	100	0
Isodrin	.05	100	0
Malathion	.25	100	0
	.1	100	0
	.05	100	0
	.025	100	0
Diazinon	.05	100	0
	.025	100	0
	.05	100	0
	.005	100	light
Chlorothion®	.002	100	0
Dipterex®	.1	100	light
	.05	100	light
	.025	100	light
	.01	100	light
	.002	100	light
Bayer 21/199	.002	100	0
Bayer 21/200	.002	25	light

(12) EPN® and other compounds: Toxicity for Anopheles quadrimaculatus (4th instar) in laboratory tests; in acetone-water suspensions: 1766

Compound	% Kill 48 Hrs At							
	.1 ppm	.05 ppm	.025 ppm	.01 ppm	.005 ppm	.0025 ppm	.001 ppm	.0005 ppm
EPN®	100	100	100	100	100	96	32	—
Sulfotepp	100	100	100	100	100	100	74	34
Parathion	100	100	100	100	100	96	56	34
Methyl parathion	100	100	100	100	100	67	—	—
O,O-Dimethyl O-(2-chloro-4-nitrophenyl) thiophosphate	100	100	100	96	86	62	62	44
Malathion	100	100	96	80	80	60	40	24
Diazinon	100	100	100	100	36	20	—	—

(12) EPN® and other compounds: Toxicity for Anopheles quadrimaculatus (4th instar) in laboratory tests; in acetone-water suspensions: (continued) 1766

Compound	% Kill 48 Hrs At .1 ppm	.05 ppm	.025 ppm	.01 ppm	.005 ppm	.0025 ppm	.001 ppm	.0005 ppm
Ethyl-o-nitrophenyl thionobenzenephosphonate	100	100	100	100	70	80	4	—
Para-oxon	100	100	100	82	50	—	—	—
O,O-Dimethyl-O-(3-chloro-4-methyl umbelliferone) thiophosphate	100	100	100	64	46	24	—	—
Chlorothion®	100	100	88	76	44	—	—	—
Potasan®	100	98	56	30	5	—	—	—
O,O-Diethyl-O-piperonyl thiophosphate	100	94	58	26	—	—	—	—
NPD	94	—	62	30	—	—	—	—
DDT	—	—	—	100	94	49	24	—

(13) Effectiveness EPN® and other substances, vs. larvae of Anopheles quadrimaculatus and A. crucians, in field experiences: 1766

Compound	% Kill 24 Hrs At Lbs/Acre Indicated 0.25	0.1	0.05	0.025	0.01	0.005	0.0025	0.001
EPN®	—	—	95	96	96	95	92	91
O,O-Dimethyl-O(3-chloro-4-methyl umbelliferone) thiophosphate	—	—	98	98	99	96	91	84
Parathion	—	—	97	97	92	99	88	—
Methyl parathion	—	100	98	83	69	51	50	—
Ethyl-o-nitrophenyl thionobenzene phosphonate	—	99	80	88	75	70	69	71
Chlorothion®	100	99	82	73	57	50	—	—
Diazinon	—	97	97	79	58	65	55	53
O,O-Dimethyl-O-(2-chloro-4-nitrophenyl)thiophosphate	—	99	72	78	49	30	—	—
NPD	100	97	84	87	79	—	—	—
Para-oxon	—	90	77	54	46	45	49	31
Sulfotepp	—	85	72	73	63	53	30	—
Malathion	90	78	79	68	60	—	—	—
O,O-Diethyl-O-piperonyl thiophosphate	—	—	78	64	75	74	45	35
Potasan®	—	77	59	72	52	—	—	—
DDT	—	—	99	48	99	98	95	92

(14) For comparative toxicity of EPN® and other compounds as acaricides consult, in this work, the general treatment titled Miticides or Acaricides.

d) EPN® vs. Bees and other beneficial insects:

(1) EPN® is toxic to bees. In some cases, poisoned bees may endanger the whole brood by returning to the hive before dying. Precautions involve the careful and proper scheduling of spray operations with regard to blooming time of bee-visited flowering crops. 874

(2) Consult the various data tabulated in this work in the section titled Bees and Insecticides.

(3) Complete elimination from sprayed crops of the following useful, predaceous insects has been reported as a result of EPN® use: 2650

(a) Nabis ferus
(b) Geocoris punctipes
(c) Coleomegilla maculata
(d) Hippodamia convergens

e) EPN® and insects (and arthropods other than insects) of public health importance:

(1) Screening tests and field tests made against mosquito larvae; flies, (particularly strains which have been selected by natural selection for resistance to the chlorinated hydrocarbons) have shown the high toxicity of EPN® for insects of public health importance and veterinary importance. (Consult data in this section for mosquito larvae and certain lice of domestic animals). However, the great toxicity of EPN® limits its use for the control of pests of public health and veterinary importance. Extreme care must be exercised and outdoor use only is presently recommended. 1801 2345 129

9) Pharmacological, pharmacodynamical, physiological, etc.; insects:

a) Consult, for details, in this work, the section titled Organic Phosphates.

(1) The high order of contact toxicity of EPN® indicates its ability to enter the insect and acarine body through the cuticula, as well as by ingestion. 2231

(2) While data specific for EPN® and its action in insects are meager, there seems ample reason to assume that the general mechanism of intoxication resembles that for other organic phosphate esters, e.g. parathion.

(3) Ability to inhibit choline esterases, thus impairing the normal systems of transmission of the nerve impulse, is assumed to underlie the toxicant action of EPN® and other organic phosphate insecticides. 2231 713

(4) Altho highly purified EPN® shows no in vitro choline esterase inhibition, it is transformed in vivo to an active inhibitor. EPN® undergoes enzymatic conversion to an active choline esterase(s) inhibitor when incubated with tissues or tissue breis, of Periplaneta americana. Gut tissue is particularly active in effecting the conversion. 2231

10) EPN® in the economic control of Insects and Acarines:

a) As acaricide:

The manufacturer on the basis of grower use, investigator field trials, and other evaluations summarizes the acaricidal usefulness of EPN® as follows: 874

(1) Vs. European red mite: Outstanding control wherever tested.
(2) Vs. Two-spotted mites: Adequate control, less spectacular than with European red mite.
(3) Vs. Willamette mite: } Good control results.
(4) Vs. Schoene mite: }
(5) Vs. Pacific mite: Good control in most instances.
(6) Vs. citrus red mite: Good—excellent control.
(7) Vs. citrus rust mite: } In limited tests, control to some degree.
(8) Vs. citrus bud mite: }
(9) Vs. clover mite (Bryobia praetiosa): Ineffective; commercial control not obtained.
(10) Vs. Paratetranychus yothersi, Petrobia latens, Septanychus texazona, spruce mites, two-spotted mites, others, on diverse host plants, control has varied with species, conditions, method of application, with reports varying from "good to excellent," "fair," "mediocre."

b) As insecticide:

(1) On pomes: Outstanding control of pear psylla, plum curculio; commercial control of apple flea weevil, red banded leaf roller; experimental promise for apple leafhopper, apple maggot, Forbes' scale grasshoppers, Japanese beetle adults, oriental fruit moth, quince curculio, round-headed apple borer, San José scale crawlers, spotted leaf miners; mediocre-ineffective control of eye-spotted bud moth, green apple aphid, oystershell scale, scurfy scale crawlers, woolly apple aphid.
(2) On drupes: Outstanding control: Plum curculio, oriental fruit moth; commercial control: Olive scale crawlers, first brood red-banded leaf roller; experimental promise: Apple pandemis, green leaf roller, lesser peach borer, mealy plum aphid, peach borer; mediocre-ineffective: Cat facing insects, green peach aphid.
(3) On citrus: Experimental promise vs: Citricola scale, thrips, leaf-rollers, mealybug, orange tortrix, scavenger worm; mediocre-ineffective vs: black scale, California red scale, green citrus aphid, purple scale, yellow scale.
(4) On corn: Promise of high effectiveness vs. European corn borer.
(5) On vegetable crops: Promising vs: Flea beetles, onion thrips, serpentine leaf miner, squash vine borer, tuber flea beetle, western spotted cucumber beetle, wireworm, "white fly"; inconclusive results vs: Cabbage worm, Colorado potato beetle, 12-spotted cucumber beetle, Mexican bean beetle, potato leaf hopper, tomato horn worm, flea beetles; mediocre results vs.: Cabbage maggot, corn earworm, potato aphid, squash bug, turnip aphid and other aphids.

c) The above comments are essentially preliminary and provisional with such an insecticide as EPN®, and it is premature to estimate its full potentialities or draw backs. Additional details may be found in the technical supplements and reports to the reference cited. Particularly may be found indications for nut crops, tobacco, forage crops, grapes, tropical and subtropical fruits.

d) Other evaluations of EPN® may be found in the section of this work titled Miticides or Acaricides and in the following references: 2864, 622, 1351, 1403, 353, 526, 118, 117, 1807, 905, 1482, 1442, 191, 1699, 727.

94

FLUORINE, FLUORIDES, FLUOSILICATES, FLUOALUMINATES

GENERAL [Refs.: 353, 2815, 1059, 757, 2226, 2120, 129, 1801]

Among inorganic insecticides, fluorine containing compounds of several general kinds have been in long and effective use. Among the more prominent of these compounds may be listed: Barium fluosilicate, cryolite (sodium fluoaluminate), sodium fluosilicate, and sodium fluoride, each of which is treated individually elsewhere in this work. General agreement is that the essential toxic principle of all these substances is fluorine, and differences of toxicity and effectiveness, as well as disadvantageous or advantageous properties with respect to phytotoxicity, hazard, etc. depend largely on the availability of the toxic principle, for example, its ready availability in soluble form. The present general treatment provides comparative data for the inorganic fluorine-containing insecticides and deals with problems and characteristics which they have in common. For bibliography of fluorine compounds as insecticides see Ref. 486.

1) Elemental fluorine; fluorine gas:

a) Fluorine gas has been tested on several insects as a fumigant with the following results: (Fumigation carried out in 100 ft³ stainless steel vault at 20°C, 1 hour exposures) 2242

Insect	% Mortality At	
	227 ppm (1g/100 ft³)	1305 ppm (5.75g/100 ft³)
Oncopeltus fasciatus (adult)	42 in 24 hrs	100 in 24 hrs
Blattella germanica (adult)	0 in 24 hrs	73 in 24 hrs
Drosophila melanogaster (adult)	100 in 24 hrs	100 in 24 hrs
Heliothrips haemorrhoidalis (adult)	22 in 24 hrs	100 in 24 hrs
Paratetranychus citri (adult)	78 in 24 hrs	100 in 24 hrs
Paratetranychus citri (egg)	14 in 7 days	24 in 7 days
Tribolium confusum (adult)	—	81 in 24 hrs
Aonidiella aurantii (adult)	7 in 21 days	96 in 21 days
Carpophilus hemipterus (egg)	50 in 6 days	80 in 6 days

Citrus seedlings, 18 inches tall, fumigated at 227 ppm, 1 hr. exposure, revealed no adverse effects 21 days after exposure; at 1305 ppm slight leaf "burn" was apparent in 24 hrs., and all leaves were withered in 10 days.

2) Fluorine compounds, toxicity for insects:

a) Sodium fluoride vs. *Periplaneta americana* (adults, ♂ 0.9 (0.7-1.15) g, ♀ 1.3 (1.0-1.9) g average body wgt) by various routes: 2219

Route	Dosage (μg/g) To Yield % Mortality Indicated					
	0%		50%		100%	
	♂	♀	♂	♀	♂	♀
Topical	160	200	250	500	350	850
Oral	100	200	300	1000	1300	3500
Injection (blood)	80	100	120	140	150	170
	For comparison: sodium arsenate ($Na_2H\,AsO_4 \cdot 7\,H_2O$)					
Topical	30	150	100	500	300	1300
Oral	80	600	250	2000	600	6000
Injection (blood)	23	35	30	50	45	70
	For comparison: acid lead arsenate (colloidal)					
Topical	200	400	500	1200	1300	2100
Oral	50	150	150	400	600	1000
Injection (blood)	200	300	300	750	750	1400

b) Various fluorine containing compounds; toxicity for *Bombyx mori* (4th instar larvae) via oral route: 2819, 459

Compound	LC_{50}, Oral, (mg/g)	g Soluble/100cc Water At 25°C
Sodium fluoride, NaF	0.11-0.15	4.054
Manganese fluoride, MnF_2	0.20-0.40	—
Lead fluoride, PbF_2	0.25-0.40	0.066
Magnesium fluoride, MgF_2	>0.57	—
Sodium fluosilicate, Na_2SiF_6	0.10-0.13; 0.09	0.762
Potassium fluosilicate, K_2SiF_6	0.07-0.10; 0.13	0.177
Barium fluosilicate, $BaSiF_6$	0.09-0.12; 0.17	0.025
Sodium fluoaluminate, Na_3AlF_6	0.05-0.07; 0.18	0.061
Potassium fluoaluminate, K_3AlF_6	0.08-0.10	0.158
Ammonium fluoaluminate, $(NH_4)_3AlF_6$	0.11-0.14	—
Acid lead arsenate (for comparison)	0.086	—

c) Various fluorine containing compounds vs. *Apis mellifera*, oral route, as suspensions or solutions at 0.36%; time to produce 50% mortality in hours; several arsenates for comparison: 812

Substance	Lethal Time_{50}, (Hrs)	Substance	Lethal Time_{50}, (Hrs)
Cryolite (natural)	8	Sodium fluoride	4
Cryolite + lime 1 : 1/2	20	Calcium fluoride	—
Cryolite + lime 1 : 1	26	Barium fluoride	8
Cryolite + lime 1 : 2	35	Iron fluoride (FeF_3)	21
Cryolite (synthetic)	4	Sodium fluosilicate	2.5
Cryolite + Bordeaux 1 :1	4	Zinc fluosilicate	4
Cryolite + Bordeaux 1 :2	4	Lead arsenate	24
Cryolite + lead arsenate 1 : 1	8	Magnesium arsenate	22
Cryolite filtered supernatant	23	Calcium arsenate	2
Cryolite (natural) 0.72% suspension	4	Sodium arsenate	2
Barium fluosilicate	4		
Potassium fluoride	4		
Ammonium fluoride	1.75		
Ammonium bifluoride (NH_4HF)	1		

(1) Lethal Time$_{50}$ correlated with amount of fluorine present, and amount available:

Compound	g/100cc Soluble in Cold Water	g Fluorine/100cc 0.36% Solution (Rounded)	Lethal Time$_{50}$ (Hrs)
NH_4HF_2	very soluble	0.24	1
NH_4F	very soluble	0.185	1.75
NaF	4.0 @ 15°C	0.163	4
KF	92.3 @ 18°C	0.178	4
NA_2SiF_6	0.652 @ 17°C	0.22	2.5
BaF_2	0.17 @ 10°C	0.08	8
CaF_2	0.0016 @ 18°C	0.175	—
Na_3AlF_6 (natural)	0.36 @ 18°C	0.18	8
Na_3AlF_6 (synthetic)	0.62 @ 18°C	0.19	4
$BaSiF_6$	0.26 @ 18°C	0.15	4

d) Fluorine compounds and other substances: Toxicity for several grasshopper species: 2611,2610

(1) *Melanoplus femur-rubrum* provided with bran baits on which insects fed *ad libitum*:

Compound	LD_{50} (mg/g)	Conc. Toxicant in bait (%)	Bait Eaten (g/g)	Toxicant Consumed (mg/g)	Survival Period
Sodium fluosilicate	0.12	1.85	0.11 (.05-.15)	2.04	9-24
Arsenious oxide	.36	1.85	.18 (.09-.27)	3.33	10-48
Monosodium arsenite	.10	1.48	.05 (.02-.09)	.74	6-24
Trisodium arsenite	.22	1.84	.04 (.01-.08)	.74	2-24
Paris green	.19	1.85	.06 (.01-.15)	1.11	4-24
Rotenone	—	1.76	.14 (.03-.22)	2.46	Recovered
Bran sans toxicant	—	0	.16 (.08-.25)	0	—

(2) LD_{50} (mg/g) for several grasshoppers, oral route, in poisoned baits:

Compound	*Melanoplus bivittatus*	*Melanoplus femur-rubrum*	*Melanoplus differentialis*	Survival Time *M. bivittatus* At 0.4 mg/g Toxicant (Hrs)
Sodium fluoride	0.04	—	0.11	—
Sodium fluosilicate	0.1	0.12	—	33
Sodium arsenite	0.015	0.10	—	20
Arsenic trioxide	0.026	0.36	0.09	33

e) Sodium fluoride and other compounds, vs. *Blattella germanica* and *Periplaneta americana*: 356,2357,2181

Compound	LC_{50} As Deposits (μg/cm^2) For *Blattella*			LD_{70} 10 Days Contact With Powder*			
	Direct Spray	Direct Dust	Environment Dust	*Periplaneta*		*Blattella*	
				μg/roach	μg/g	μg/roach	μg/g
Chlordane	1.7	2.0	0.6	—	—	—	—
Lindane	2.8	0.8	0.2	72	69	3.6	31
DDT	40.0	15.0	2.5	37	36	25	217
Pyrethrins	—	—	—	10.8	10.4	5	43
Sodium fluoride	—	130.0	40.0	1833	1763	158	1375

*Insects entering treated area *ad libitum*.

f) Fluorine compounds and other substances vs. *Blattella germanica* (adult) treated with dust formulations in pyrophyllite by the Settling Chamber Method. 1234

Compound	% Active Ingredient	*B. germanica* ♂		*B. germanica* ♀	
		% Mortality	Survival Time (Hrs)	% Mortality	Survival Time (Hrs)
Sodium fluosilicate	25	100	45.6	49	77.0
Sodium fluoride	10	92	34.6	48	63.5
Sodium fluoroacetate	1.0	100	19.7	90	42.5
Pyrethrum marc (Powell)	10	0	—	0	—
Toxaphene®	10	100	15.0	100	22.3
Toxaphene®	5	100	24.3	100	40.1
Sabadilla	10	98	28.7	75	52.2
Sabadilla	50	100	11.8	100	22.7
Sabadilla + 50% Pyrethrum marc	10	100	33.9	57	54.8
Sabadilla + 50% Boric acid	10	100	64	40	73.7
Sabadilla + 50% Sulfur	10	76	45	12	—
Chlordane	2	100	40.6	98	68.8
Chlordane	1	100	52.8	82	84.5
BHC	1	100	33.3	100	55.3
BHC (Merck)	1	100	31.1	100	47.8

f) Fluorine compounds and other substances vs. Blattella germanica (adult) treated with dust formulations in pyrophyllite by the Settling Chamber Method. 1234

Compound	% Active Ingredient	B. germanica ♂		B. germanica ♀	
		% Mortality	Survival Time (Hrs)	% Mortality	Survival Time (Hrs)
BHC (DuPont)	1	66	52.8	20	70.0
BHC + 75% Pyrethrum marc	1	100	28.0	100	52.4
BHC (Merck)	0.5	100	38.3	100	65.9
BHC + 50% Pyrethrum marc	0.5	100	27.7	98	62.1

g) Various fluorides vs. Culex quinquefasciatus (larvae); time required for 1 : 100 concentrations in the medium to yield 50% mortality: 2100

Compound	Lethal Time $_{50\%}$ At 1 : 100 Concentration (Hrs)
Calcium fluoride	84
Magnesium fluoride	54
Strontium fluoride	55
Copper fluoride	6
Barium fluoride	3
Potassium fluoride	1.5

3) Phytotoxicity:

- a) Fluorine compounds, for use as insecticides on plants, must be selected with regard to high degree of insolubility in water because of the extreme toxicity of soluble fluorine to plants. Thus, sodium fluoride is entirely unsuitable and extremely hazardous for use on plants. 353, 2815
  - (1) Cryolite, (sodium fluoaluminate), is the safest of the fluorine containing inorganics for use on plant foliage, because of its low solubility combined with high toxicity for insects. Orange foliage withstands repeated applications of 0.15% suspensions. Damage may be done even by cryolite to pome fruits and peaches. 90% of tobacco plants root-dipped in 2.5% cryolite, to control root borer, showed damage. Used in soil at 3000 lbs/acre, cryolite had no deleterious effect on lima beans, or bell peppers. 2815, 84, 2649, 2106, 2797, 2795
- b) Sodium fluoride, tested on sand cultures of lemon plant cuttings at 1, 25, 50, 100, 200, 400 ppm as fluoride: At 400 ppm severe leaf injury and defoliation when added as NaF (or KF). At 400 ppm tip burn, loss of chlorophyll, decrease in leaf size of orange cuttings. 82
- c) The fluosilicates are more hazardous to foliage than is acid lead arsenate. 2815
  - (1) Sodium fluosilicate as 0.5% suspension did not damage young foliage of orange trees; as dusts at 16 lb/acre severe scorching damage appeared on sugar cane, with a marked drop in yield. 2649, 1579
  - (2) At 1500 lbs/acre on various blue grasses sodium and barium fluosilicates proved harmless while soluble fluorides proved intensely phytotoxic. 2027, 2307
  - (3) In moderate doses sodium and barium fluosilicates severely burn grape foliage, and peach tree foliage is unusually susceptible to damage by these compounds. 2106
  - (4) In the soil at 150 lb/acre sodium fluosilicate is said to stimulate plant growth. No plants appear to be harmed by 300 lbs/acre. 2103
  - (5) Sodium fluosilicate hydrolyzes to produce soluble phytotoxic compounds; lime decreases the amount of soluble fluorine and the toxic hazard is lessened. 485

4) Pharmacological, pharmacodynamic, physiological, etc.:

- a) The fluorides, fluosilicates, fluoaluminates, are general protoplasmic poisons, toxic to virtually all plant and animal life. As insecticides they exercise effective toxic action by topical contact and as stomach poisons. 353, 2815
- b) From the standpoint of toxic residues, danger of accidental intake, contamination of food and water, these are among the most dangerous insecticides. However, they are, from the point of view of hazard, safer than lead arsenate. Their toxicity to animals is in direct proportion to fluorine content and availability. 2911
  - (1) Tolerance limits on apples as fluorine (1938) = 2.8 ppm or 0.02 grain/lb. Apples sprayed with barium fluosilicate show, before washing, an average residue of 5.6 ppm. 2815
- c) The main hazard is that of ingestion by mistaking these compounds for common comestibles e.g., sugar, salt, baking powder, etc. The toxic dose for man of sodium fluoride, for instance, is ca. 5 grams. 2815
- d) At a level of 900 ppm fluoride (derived from sodium fluoride or sodium fluosilicate) most animals are killed in 10 days; calcium fluosilicate and sodium fluoaluminate to yield the same effect would have to be given at 40,000—50,000 ppm. 788, 2888
- e) In insects:
  - (1) Fluorine poisoning in insects is associated with a definite mid-gut pathology shown by destructive changes in the epithelium. NaF in Prodenia induces necrosis, sloughing of epithelium, with disintegration of the nucleus and alterations in the cytoplasm. Similar effects have been observed in Vanessa (larvae) and Locusta. Sodium fluosilicate is less potent in its mid-gut effects in case of Locusta, and yields no histopathology in Pieris rapae, Lymantria dispar (larvae). Barium fluosilicate induces no mid-gut histopathology in Prodenia eridania (larvae). 3349, 2510
  - (2) Symptoms of intoxication with fluorine containing compounds:
    - (a) Periplaneta, Blattella, contact poisoning with NaF: Unease, irritability, followed by torpor with sudden spasms and a gradual decline of all activity to death in 4-48 hours after exposure to NaF dusts. 2750

(b) Prodenia (larva) after oral administration NaF: Rearing, twisting of head and thorax, turning over and over, twisting of whole body, sometimes with regurgitation. After barium fluosilicate: Sluggishness with occasional spasms, followed by gradually oncoming death in flaccid paralysis; no histopathology. 3349

(3) Fluoride ion inhibits esterases, brings about protoplasmic damage with precipitation of calcium; acid phosphatases are inhibited with damage to glycolytic phosphorylation; inhibition of phosphoroglyceric enolase with glycolytic arrest at the triose stage. Blocks the iron component of catalase. 223 164 3107

(a) NaF perfusion of muscle and fat body, of Carpocapsa (larva) leads to decline of oxidative glycolytic metabolism with a 2-fold increase in the respiratory quotient. 1243

(b) Addition of NaF to Passalus tissue preparations leads to decreased catalase activity, slightly enhanced dehydrogenase and phenoloxidase activity. 2749

(c) Partial inhibition by NaF of bee and cockroach nerve choline esterase and of mid-gut lipase (Calliptamus) is reported. 2600 2762

f) In higher animals:

(1) Actual amount of fluorine absorbed depends on solubility, physical form of the ingested salt, and amount of calcium ions in alimentary tract. Some complex inorganic compounds, even though soluble and absorbable, may not yield F^- ions. Ca. 90% of the more soluble fluoride salts are absorbed vs. 40-80% of the less soluble salts. 90-100% of absorbed fluoride is excreted in sweat and urine. Excreted in milk, it may cause death of nursling rats. 1920

(a) Affinity for teeth and bone: Concentration in bone vs. soft tissues may be 200 to 500 : 1. 2061,2205,2760

(2) Excretion of F^- is adequate until intake equals 3 mg or more per day or 4 ppm. in drinking water; at 4.5-20 ppm intake per day 35%-60% of absorbed fluorine is retained. Soft-tissue-stored fluorine is quickly excreted via urine, but bone-and tooth-held fluorine is released only over months or years. 1919

(3) Toxicity:

(a) 230-450 mg yielded severe symptoms for 36 or more hours if retained; lowest recorded fatal dose (man) = 2 grams. 851

(b) In rabbits, NaF LD_0 = 75 mg/k, LD_{80} = 87.5 mg/k, LD_{100} = 90 mg/k intravenous; MLD oral dosage = 0.5 g/k. 1941

(4) Effects, man:

(a) Initial effects: Gastrointestinal disturbances, epigastric pain followed by muscle weakness, clonic convulsions, circulatory collapse, myocardial failure. Rigor rapidly follows death. 851

(b) Autopsy reveals: Inflammation, petechiae on oesophagus, stomach, small intestine with blood in stomach. Cerebral, pulmonary, hyperaemia; pin-point hemorrhage may occur. Albuminuria, hydropic degeneration of kidneys, liver, may occur. 2312

(c) Increases capillary permeability in small doses; yields gross damage in large doses. Peripheral neuritis may follow survival of fluoride poisoning. 851

(d) A pernicious anaemia-like syndrome has been noted in dogs. 1942

(5) Toxicity of fluosilicates is attributed to liberation of F^- ions.

(6) Local action of NaF includes gastroenteritis after ingestion; 2% solutions destroy superficial cells of mucosae. 851

(7) Mechanisms of toxic action:

(a) Hypocalcemia has been suggested. 1268

(b) Inhibition of enzymatic action: Inhibition of anaerobic glycolysis in muscle homogenates and with yeast is known, with adenylic acid + $MgCl_2$ protecting against this action. Esterases (lipase, phosphatase, choline esterase) are inhibited. 851

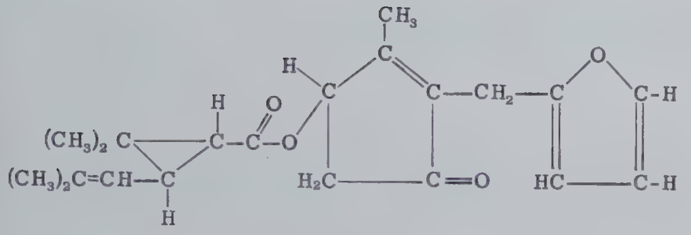
(8) Chronic toxicity: 851

(a) Confined to teeth and bone. Mottling of teeth is a first sign of chronic toxicity. "Radiopacity" of bones occurs, but without pathology or disability in low dosages. With increasing dosages, deformation of bones occurs, with thickening, roughness, and exostoses, particularly at muscle attachment points, which may inhibit movement, especially of the spine.

(9) Insecticides and rodenticides containing fluorine compounds are almost solely responsible for human fluoride poisonings. 851 1221

95

FURETHRIN (DL-2-(2-Furfuryl)-3-methyl-2-cyclopenten-4-ol-1-onyl DL-cis-trans-chrysanthemate; DL-Furfurylrethronyl DL-cis-trans-chrysanthemate; DL-2-(2-Furfuryl)-4-hydroxy-3-methyl-2-cyclopenten-1- one ester of DL-cis-trans-chrysanthemum monocarboxylic acid)



GENERAL

[Refs.: 2138,2139,2231,2120,964,1161,2119]

A synthetic pyrethroid (also consult pyrethrum, pyrethrin, allethrin, cyclethrin) of great promise; first synthesized in Japan using furfurylacetone as a point of departure to obtain furethrolone which is condensed with chrysanthemum monocarboxylic acid chlorides to yield furethrin. Due to the relative abundance of furfurylacetone, furethrin may be more economically produced than allethrin, q.v., another synthetic pyrethroid which furethrin closely resembles in insecticidal behavior. Although similar in action to allethrin, cyclethrin and the natural pyrethrins, furethrin yields slightly less kill of Musca domestica at equivalent dosages than do allethrin and the pyrethrins. Furethrin appears to be relatively more effective in "knockdown" than is allethrin. Versus Aëdes spp. and Periplaneta americana the order of effectiveness of furethrin parallels that of allethrin. The d-trans-chrysanthemic acid isomer is 2 times as toxic for Musca as is furethrin, the racemic mixture.

PHYSICAL, CHEMICAL

A pale yellow liquid; b.p. 187°-188°C at 0.4 mm Hg; $n_D^{25^\circ}$ 1.5205; insoluble or virtually insoluble in water; soluble in refined kerosene. The foregoing properties apply to the technical product.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) No data on the acute, sub-acute or chronic toxicity of furethrin for higher animals are available to this compilation. It may be assumed that toxicity is not strikingly different from that of allethrin or natural pyrethrins, q.v. The same is true for mode of action and pharmacological and pharmacodynamical properties in general.

2) Toxicity for insects:
   a) Comparative toxicity of furethrin (2 samples), the d-trans-chrysanthemic acid isomer of furethrin and natural pyrethrins for Musca domestica as direct contact sprays in refined kerosene: 1161

Compound	LC_{50} (mg/cc)	Relative Toxicity (Pyrethrins = 1.0)
Furethrin (U.S.D.A. Sample)	1.877 ± 0.09	1.109 ± 0.075
Furethrin (Japanese Sample)	2.872 ± 0.128	0.725 ± 0.047
Furethrin (d-trans acid isomer)	1.087 ± 0.05	1.915 ± 0.127
Pyrethrins	2.082 ± 0.1	1.0 (standard)

   b) Mortality and "knockdown" of Musca domestica (adult) with various concentrations of furethrin samples in refined kerosene; application as direct contact sprays, turntable method: 1161

Compound	Concentration (mg/l)	% Mortality 24 Hrs.	% "Knockdown" 10 Min.
Furethrin (Japanese Sample)	8	84.4	100
" "	4	57.9	100
" "	2	35.5	100
" "	1	19.8	100
Furethrin (U.S.D.A. Sample)	8	94.0	100
" "	4	79.1	100
" "	2	52.4	100

b) Mortality and "knockdown" of Musca domestica (adult) with various concentrations of furethrin samples in refined kerosene; application as direct contact sprays, turntable method: (continued) 1161

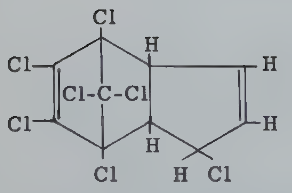
Compound	Concentration	% Mortality 24 Hrs.	% "Knockdown" 10 Min.
Furethrin (U.S.D.A. Sample)	1	23.5	100
Furethrin (d-trans-acid isomer)	4	96.5	100
" "	2	70.3	100
" "	1	47.3	100
" "	0.5	23.6	100
Pyrethrins	8	93.5	100
"	4	77.6	100
"	2	42.4	100
"	1	22.8	100

(1) Furethrin is stated to be one third as toxic for Musca domestica as allethrin. 1161

c) For screening test data indicating effectiveness toward Pediculus humanus corporis (adults, eggs), mosquito larvae, flies, and as a repellent for mosquitoes (Aëdes aegypti) consult Ref. 1801.

96

HEPTACHLOR (1, 4, 5, 6, 7, 8, 8-Heptachloro-3a, 4, 7, 7a-tetrahydro-4, 7-endomethanoindene; 3, 4, 5, 6, 7, 8, 8a-Heptachlorodicyclopentadiene; Heptachlorotetrahydro-4, 7-methanoindane; Velsicol 104; E-3314.)

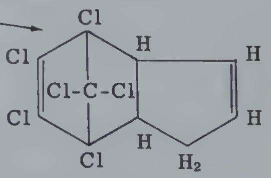


Molecular weight: 373.239

GENERAL

[Refs.: 353, 2231, 2120, 129, 2093, 1756, 1757, 1988, 3199, 270, 1504, 1634, 2692, 371, 1828, 2577, 670, 954, 2427, 3266, 1152, 1996]

One of a general group of compounds bearing, among others, the designation 'cyclodiene insecticides'. This group includes in addition to heptachlor: Aldrin, chlordane, dieldrin, endrin, isodrin, toxaphene, q.v.. Each is a highly chlorinated, cyclic hydrocarbon with an endomethylene bridge in its structure. All (save toxaphene) are synthesized by the Diels-Alder diene reaction. Heptachlor was first isolated from technical chlordane, being closely related to that substance. Each is derived from the chlorination of chlordene (4,5,6,7,8,8-hexachloro-3a,4,7,7a-tetra-hydro-4,7-methanoindene) the result being in the case of heptachlor a heptachloro-compound, in the case of chlordane an octachloro-compound. It is of interest to note that chlordene, is but weakly insecticidal (300 times less effective vs. Oncopeltus fasciatus than heptachlor). Heptachlor manifests toward Musca domestica and Melanoplus differentialis the same high toxicity as γ- BHC (lindane), having been characterized as 4-5 times as insecticidal as technical chlordane. Trans-chlordane (10 times more toxic than cis-chlordane for O. fasciatus) is not quite as toxic for O. fasciatus as is heptachlor. While being more toxic by a factor of ca. 5 than technical chlordane for M. domestica, heptachlor is reported as lacking in effective "knockdown" power. Heptachlor is toxic to insects by contact, ingestion and, to some extent, by fumigation. More volatile than DDT, heptachlor is consequently less residually effective. Heptachlor has proved its effectiveness against such pests as grasshoppers, various soil insects for example, cutworms, rootworms, wireworms, some cotton insects (ineffective, however, for pink bollworm) onion thrips, alfalfa weevil, plum curculio, black-fly larvae, cockroaches, flies and mosquitoes. Toward the two latter, the toxicity of heptachlor must be qualified by the resistance shown by certain "populations" selected specifically by exposure to heptachlor, and by cross resistance shown by strains selected by exposure to other chlorinated hydrocarbons for instance, DDT. The potency of heptachlor may be sufficiently indicated by the control of grasshoppers achieved with sprays or dusts at the rate of 2-4 ounces per acre, cotton weevil by 0.25 lb per acre, plum curculio by 3 lbs wettable powder (25% heptachlor) per 100 gallons water, soil insects by 0.5-2 lbs per acre, depending on soil type.



PHYSICAL, CHEMICAL

A white crystalline solid (pure); a soft, waxy solid (technical); m.p. (pure) 95°-96°C; m.p. (technical) 46°-74°C; b.p. (pure) 135°-145°C at 1-1.5 mm Hg; $d^{9^\circ}_{9^\circ}$ (technical) 1.57-1.59; v.p. (pure) 3×10^{-4} mm Hg at 25°C (estimated); odor: Mild, camphor- or cedar-like; the technical product contains ca. 67% heptachlor and 33% related substances e.g. α-chlordane; virtually insoluble in water; readily soluble in paraffinic and aromatic hydrocarbons:

Solvent	g/100 cc Solvent Soluble at 26°C
Acetone	75
Benzene	106
Carbon tetrachloride	112
Cyclohexanone	119
Deodorized kerosene	18.9
o-Dichlorobenzene	100
Ethanol	4.5
Hexane	33
Kerosene	15
Methylated naphthalenes	82.5
Pentane	23.5
Xylene	102 ;

stable toward heat to 150°-160°C, and toward light, air, moisture, alkalis, acids; not readily dechlorinated.

a) Formulations: As wettable powders, dusts, emulsifiable concentrates (customarily at 2 lbs per gallon, U. S.).

TOXICOLOGICAL

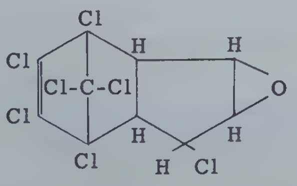
1) General: Toxicologically, for higher animals, heptachlor is comparatively little known. It is toxic and distinctly hazardous by all portals of entry to the animal body: Ingestion, inhalation, via the skin. The residue hazards are initially high on food and forage crops but, at the insecticidal rates of application, little remains as residue after 3 weeks of exposure. Thus, application to cow-peas within 10 days of harvest is not recommended nor, within 5 days of harvest, or hand picking, is application to onions or cotton recommended. By analogy with related insecticides, all precautions in handling and application, avoidance of contact with the skin, inhalation of dusts and mists, contamination of food and forage should be de rigueur. Also, by analogy, the hazard to wild life, e.g. game birds, may tentatively be rated high. About 2 times as toxic to higher animals as technical chlordane. Cutaneous danger levels ca. one-half those of chlordane. 3199,1298 129, 780 1949,1427

2) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	135		1014
Rat	or	LD_{50}	90	Tremors, convulsions within 1/2-1 hr; death after 48 hrs.	1949,1951 1954
Mouse	iv	LD_{100}	40	As heptachlor.	1954, 707, 709
Mouse	iv	LD_{100}	10	As heptachlor epoxide.	707, 709
Rabbit	ct	LD_{50} approx.	2000	Single application; dry powder.	1952
Rabbit	ct	Toxic	780	Single application; in solution.	1952
Mouse	or	LD_{50}	68		1014
Guinea Pig	or	LD_{50}	116		1014

3) Sub-acute, sub-chronic and chronic toxicity; higher animals:
   - a) Given in the diet to dogs at 5 mg/k/day, brought death (within 13, 21 days) of the 2 tested subjects. 1953
   - b) Given in the diet to dogs at 1 mg/k/day, brought death to 3 of 4 tested subjects in from 265-424 days. 1952
   - c) Cutaneous application to rabbits in solution at 20 mg/k daily for 14 days, caused death of all subjects. A marked cumulative action is indicated.
   - d) Moderately irritating to the skin of experimental animals. 1952
   - e) Rats, given 125 ppm in diet: Death within a few days. 1014

4) Accummulation of heptachlor and derivatives in the animal body: 706, 709
   - a) Fate of heptachlor in the body: 710,1597
     - (1) In dogs and rats orally administered heptachlor is converted rapidly to the highly toxic epoxide: 707



(one of 8 possible stereoisomers)

in which form it is stored in the body fat where it accummulates. It is interesting to note that the same conversion takes place in Musca domestica. Only at high levels of feeding can unconverted heptachlor be found in the fat of dogs.

(2) At 30 ppm in the diet, rapid accummulation of heptachlor epoxide occurs in the fat of rats; a maximum is reached in 2-4 weeks but disappearance requires 12 weeks. Storage of heptachlor epoxide is demonstrable at dietary levels of 0.3 ppm (♀ rats) and 1 ppm (♂ rats).

(3) In milk cows, given 3 mg/k/day for 14 days, heptachlor epoxide appeared in milk up to 1.8 ppm, in butterfat to 44 ppm, and complete disappearance did not take place until 51 days after the last feeding of heptachlor.

5) Pharmacological, Pharmacodynamical, Physiological, etc.; Higher Animals:

a) The above mentioned conversion of heptachlor to heptachlor epoxide in the animal body, and the demonstra- 706
tion that heptachlor epoxide is 4 times as toxic to the mouse as heptachlor by the intravenous route, suggests 709
the metabolic "activation" or enhancement of toxicity of heptachlor by epoxidation to a highly toxic meta- 710
bolite able to accumulate and be stored in the fat, but not to any extent in other tissues. 1597,707,3199

b) Heptachlor in multiple dose (chronic, sub-acute) administration produces hepatic damage like other 3199
chlorinated hydrocarbons.

c) Neurotoxic action is suggested not only by analogy with related compounds but by the above mentioned symp- 1949
toms of tremors and convulsions many hours prior to death and shortly after administration of acute oral 1951
dosages. 1954

6) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Anopheles quadrimaculatus (larva)	Medium	MLD_{100} 24 hr	0.025 ppm	At 0.01 ppm gave 79% kill in 24 hr.	2020
Blabera fusca (adult)	inj	MLD < 7 da	1.6 μg/g	In acetone-triton solution.	1986
Blabera fusca (adult)	inj	Max Td D*7 da	5.0 μg/g	* Maximum Tolerated Dose; in acetone-triton sol.	1986
Blattella germanica (adult ♀) chlordane non-R	inj	LD_{50}	9.07 μg g		431
Blattella germanica (adult ♀) chlordane non-R	inj	LD_{90}	19.85 μg/g		431
Blattella germanica (adult ♀) Corpus Christi chlordane-R	inj	LD_{50}	174.21 μg/g	$\frac{LD_{50}\text{ R strain}}{LD_{50}\text{ non-R}}$ = 19.21, relative resistance.	431
Blattella germanica (adult ♀) Corpus Christi chlordane-R	inj	LD_{90}	1509.3 μg/g	$\frac{LD_{90}\text{ R-strain}}{LD_{90}\text{ non-R}}$ = 76.04, relative resistance.-	431
Chrysops discalis (adult)	Topical	LD_{50} (estimate)	40 μg/fly		2707
Chrysops discalis (adult)	Topical	LD_{90}	200 μg/fly		2707
Dacus dorsalis (adult)	Topical	LD_{50}	0.015 μg/fly		2692
Musca domestica (adult)	Topical	LD_{50}	1.6 ; 1.7 μg/g	Relative toxicity (chlordane = 1) 0.43.	2231
Musca domestica (adult)	Contact Spray	LC_{50} 24 hr	0.052 mg/cc	Turntable method; KD 10 min. at LC_{50} 24 hr = 0.	2033
Musca domestica (adult)	Contact Spray	LC_{50}	0.114 ± .009mg/cc	Space spray by Campbell turntable; in kerosene.	1152
Musca domestica adult, DDT-non R strain	Topical	LD_{50} 24 hr	0.03 μg/fly	DDT LD_{50} = 0.02 μg/fly.	2098
Musca domestica DDT-R, Riverside strain	Topical	LD_{50} 24 hr	0.07 μg/fly	DDT LD_{50} = 0.5 μg/fly.	2098
Musca domestica DDT-R, Ontario strain	Topical	LD_{50} 24 hr	0.07 μg/fly	DDT LD_{50} = 0.5 μg/fly.	2098
Musca domestica DDT-R, San José strain	Topical	LD_{50} 24 hr	0.07 μg/fly	DDT LD_{50} = 0.7 μg/fly.	2098
Musca domestica DDT-R, Bellflower strain	Topical	LD_{50} 24 hr	0.06 μg/fly	DDT LD_{50} = 10.0 μg/fly.	2098
Musca domestica DDT-R, Pollard strain	Topical	LD_{50} 24 hr	1.15 μg/fly		371
Musca domestica DDT-non R, Laboratory strain	Topical	LD_{50} 24 hr	0.032 μg/fly	At 60°F; chlordane LD_{50} 24 hr = 0.12 μg/fly.	2692,371
Musca domestica DDT-R-Auburn strain	Topical	LD_{50}	13(11-17)μg/fly	Overlap of fiducial limits (0.95) values indicates no significant difference in heptachlor susceptibility of two strains.	2110
Musca domestica DDT-R-Auburn strain	Topical	LD_{50}	855.79 μg/g		2110
Musca domestica DDT-non R, Orlando strain	Topical	LD_{50}	11(8.75-15) μg/fly		2110
Musca domestica DDT-non R, Orlando strain	Topical	LD_{50}	955.68 μg/g		2110
Melanoplus differentialis (adult)	Topical	LD_{50}	1.6; 2.6 μg/g	In acetone solution.	3267
Melanoplus differentialis (adult)	or	LD_{50}	4.4; 6.0 μg/g	As a deposit (from solution) on leaves.	3267
Oncopeltus fasciatus (adult)	Topical	LD_{50}	31.0 μg/g		2231
Periplaneta americana (adult)	Topical	LD_{50}	1.0 μg/g		2231
Protoparce sexta (5th instar)	Topical	LD_{50}	1058 μg/larva	Large larvae [5.4 (4.1-7.5)g.]	1306
Protoparce sexta (5th instar)	Topical	LD_{90}	4005 μg/larva		1306
Rhagoletis completa (adult)	Topical	LD_{50}	0.015 μg/fly		2692

b) Comparative toxicity, heptachlor and other compounds for insects: 2692

(1)

Insecticide	Topical LD_{50} (μg/insect) For Musca domestica	Rhagoletis completa	Dacus dorsalis
Heptachlor	0.032	0.06	0.015
Dieldrin	.031	.025	.024
Aldrin	.035	.066	.023
Lindane	.01	.027	.025
Parathion	.015	.011	.012
DDT	.033	.86	.23
Methoxychlor	.068	.15	1.0
DDD	.13	.18	>1.0

(2) Toxicity of heptachlor and other compounds for certain insects exposed to residues (from acetone solutions) on filter paper: 2692

Insecticide	μg/cm²	% Mortality 96 Hrs. For Blattella germanica	Pogonomyrmex barbatus	Tribolium confusum
Heptachlor	13	100	100	—
"	1.3	90	80	69
"	0.13	30	80	9
Chlordane	13	100	75	—

(2) Toxicity of heptachlor and other compounds for certain insects exposed to residues (from acetone solutions) on filter paper: (continued) 2692

Insecticide	μg/cm^3	% Mortality 96 Hrs. For		
		Blattella germanica	Pogonomyrmex barbatus	Tribolium confusum
Chlordane	1.3	55	60	12
"	0.13	5	40	3
p,p′-DDT	2550	0	—	—
"	525	—	0	—
Lindane	13	100	100	—
"	1.3	90	65	43
"	0.13	0	60	1

(3) Toxicity of heptachlor and other insecticides as residues on dipped oranges, for Heliothrips haemorrhoidalis: 2692

Insecticide	Concentration Of Solution (%)	% Mortality 24 Hrs.
Heptachlor	0.0025	100
"	.001	87
"	.0005	62
"	.00025	14
"	.0001	2
Chlordane	.01	96
"	.0075	85
"	.005	50
"	.0025	39
"	.001	18
DDT	.01	100
"	.001	46
Hexachlor	.1	100
"	.01	73
"	.005	60
Octachlor	.05	98
"	.025	97
"	.01	96
"	.005	86
Enneachlor	.05	100
"	.025	89
"	.01	79
"	.005	58

(4) Toxicity of heptachlor and other substances vs. Entomobrya sp., exposed to contact with filter paper deposits at 2.55 μg/cm^2: 2692

Insecticide	% Dying At			
	30 min	1 hr.	2 hrs.	4 hrs.
Heptachlor	0	41	62	100
Chlordane	0	7	14	63
DDT	0	6	6	21
Control	0	0	0	9

(5) Toxicity of heptachlor and DDT vs. Aonidiella aurantii (crawling stage). Exposure to residues of 20% xylene solutions as water emulsions: 2692

Concentration Of Xylene Solution (cc/l)	% Mortality Yielded By	
	Heptachlor	DDT
10	0	100
5	—	100
2	—	100
1	—	100
0.5	—	99

(6) Toxicity of heptachlor and other compounds vs. Listroderes costirostris obliquus exposed to residues on impregnated filter paper: 2692

Insecticide	μg/cm^2	% Uncoordinated : Dead At			
		11 hrs.	24 hrs.	54 hrs.	101 hrs.
Heptachlor	105	0 : 0	100 : 0	100 : 60	100 : 90
Chlordane	105	0 : 0	100 : 0	100 : 80	100 : 100
DDT	105	0 : 0	0 : 0	40 : 15	80 : 70
Control	0	0 : 0	0 : 0	0 : 0	0 : 0

(7) Heptachlor and other insecticides vs. *Archips argyrospila*, exposed to lemon leaves dusted with 25% dusts: 2692

Insecticide	μg/cm^2	% Mortality At			
		17.5 hrs.	32.5 hrs.	54 hrs.	90 hrs.
Heptachlor	8	0	28	64	92
Chlordane (tech)	8	4	28	68	100
DDT (tech)	8	56	100	—	—
Control	0	0	8	15	50

(8) Heptachlor and other compounds vs. *Apantesis proxima* (mature larva): 2692

Exposed To	Insecticide	% Mortality At				
		2 days	3 days	5 days	7 days	10 days
105 μg/cm^2 on filter paper	Heptachlor	12	32	65	86	100
	Chlordane	10	27	72	87	95
	DDT	0	0	3	5	8
2.5% dust at 20 μg/cm^2	Heptachlor	20	30	60	65	75
	Chlordane (tech)	15	35	80	80	80
	DDT (tech)	55	55	60	65	75
1.25% poison bran at 1 g/30 larvae	Heptachlor	7	37	67	90	90
	Chlordane (tech)	13	37	63	77	83
	DDT (tech)	20	37	43	43	47

(9) Heptachlor and other insecticides vs. *Phryganidia californica* (larva) exposed to impregnated filter paper: 2692

Insecticide	μg/cm^2	% Moribund At		
		41.5 hrs.	67 hrs.	97.5 hrs.
Heptachlor	105	93	97	100
"	10.5	54	89	93
Chlordane	105	84	100	100
"	10.5	12	21	58
DDT	105	18	72	93
"	10.5	15	66	77
Control	0	0	0	0

(10) Heptachlor and other compounds vs. *Phoenicia sericata* (adult) exposed to residues on impregnated filter paper: 2692

Insecticide	μg/cm^2	% (24 Hrs.)	
		"Knockdown"	Mortality
Heptachlor	0.1	100	70
"	.01	70	22
"	.001	5	5
Chlordane	.1	95	58
"	.01	42	11
"	.001	0	0
DDT	1.0	61	44
"	.1	21	21
"	.01	22	11

Fumigant action from impregnated paper (0.4 cc solution) insects not in direct contact with impregnated paper:

Insecticide	% Conc. Of Solution	Time (Hrs) For	
		50% "Knockdown"	50% Kill
Heptachlor	0.01	2.6	3.6
"	.001	4.9	6.3
Chlordane	1.0	8.4	9.1
Lindane	.01	1.1	2.2
"	.001	22.7	22.7
DDT	5.0	22.8	23.2
Control	0	22.2	22.7

(11) Heptachlor and others vs. *Melanoplus differentialis* (adult) oral and topical administration: 3267

Insecticide	LD$_{50}$, Topical (μg/g)	LD$_{50}$, Oral (μg/g)
Heptachlor	2.6; 1.6	6.0; 4.4
DDT	>3300; 9380.0	>1350; 2579.0; 1170.0*
Toxaphene®	73.9; 61.0	75.0; 91.5

(11) Heptachlor and others vs. Melanoplus differentialis (adult) oral and topical administration: (continued) 3267

Insecticide	LD$_{50}$, Topical (μg/g)	LD$_{50}$, Oral (μg/g)
Chlordane	16.3; 9.8	21.8; 12.0
Lindane	1.6; 3.4	6.6; 6.7
Aldrin	1.8	2.3
Dieldrin	1.4	3.7
Parathion	0.7; 0.8	6.0; 8.9
TEPP	4.4	—
HETP	18.4	—

* As a colloidal suspension applied directly to mouth parts.

(12) Toxicity of heptachlor and other compounds vs. 2 strains of Musca domestica (adult); Auburn strain (DDT-R) 14 times as resistant as Orlando strain (DDT-non-R). Topical application as acetone solutions: 2110

Insecticide	Auburn Strain			Orlando Strain		
	LD$_{50}$ (μg/fly)	0.95% limits	LD$_{50}$ (μg/g)	LD$_{50}$ (μg/fly)	0.95% limits	LD$_{50}$(μg/g)
Heptachlor	13	(11-17)	855.79	11	(8.75-15)	955.68
Chlordane	29	(12-57)	2791.3	42	(42 -84)	3586.8
Methoxychlor	2.33	(2.03-2.53)	135.18	1.93	(1.33-2.33)	127.49
Chlorothion®	0.14	(0.1-0.2)	10.52	0.21	(0.19-0.25)	16.89
Diazinon	0.06	(0.05-0.07)	3.01	0.1	(0.09-0.11)	6.15
Experimental 4124	0.03	(0.03-0.03)	2.75	0.02	(0.02-0.03)	1.73

(13) Toxicity of heptachlor and other substances vs. Musca domestica (larvae); applied as emulsions Laboratory tests:* 1326

Insecticide	% Mortality At mg Active Ingredient/k Medium					
	50 mg	20 mg	15 mg	10 mg	5 mg	2 mg
Heptachlor	—	100	—	—	100	90
DDT	100	—	—	—	—	—
Methoxychlor	25	—	—	—	—	—
Toxaphene	100	100	—	100	75	0
Lindane	—	99.5	—	60	—	—
Chlordane	—	—	100	—	—	75
Aldrin	—	—	100	100	100	97.5
Dieldrin	—	100	—	100	100	94
Dilan	99.5	100	—	100	5	—

*Field tests discouraging; control obtainable in places where breeding could be detected but not elsewhere.

(14) Heptachlor and other compounds vs. Musca domestica adults, as contact sprays applied by modification (turntable) of the Peet-Grady method: 2033

Insecticide	mg/cc Spray To Give 50% Kill In 24 Hrs.	% "Knockdown" In 10 Minutes At Concentration Yielding 50% Kill In 24 Hrs.
Heptachlor	0.052	0
Dieldrin	.017	0
Parathion	.02	0
Methyl parathion	.025	0
Lindane	.046	0
Aldrin	.056	0
TEPP	.069	ca 70
Chlordane	.25	0
DDT	.35	0
Malathion	.48	0
Toxaphene®	.68	0
Tetrapropyl dithiopyrophosphate	.69	0
Dilan	.72	ca 30
Isolan	1.15	100
Allethrin	1.5	100
Pyrolan	5.5	100

(15) Heptachlor and others vs. the chlordane non-R and chlordane-R (Corpus Christi) strains of Blattella germanica. Adult ♀♀, by injection: 431

Insecticide	Chlordane non-R		Chlordane-R		$\frac{\text{LD}_{50}\text{-R}}{\text{LD}_{50}\text{-non-R}}$	$\frac{\text{LD}_{90}\text{-R}}{\text{LD}_{90}\text{-non-R}}$
	LD$_{50}$ (μg/g)	LD$_{90}$	LD$_{50}$ (μg/g)	LD$_{90}$		
Heptachlor	9.07	19.85	174.21	1509.3	19.21	76.04
Aldrin	26.46	70.06	127.61	1113.6	4.82	15.89
Chlordane	81.29	144.27	1117.5	4648.8	13.76	32.22
Dieldrin	6.59	17.35	68.37	502.49	10.37	28.54
Lindane	1.01	2.57	23.13	75.02	22.72	29.19

(16) Heptachlor and other insecticides vs. *Blabera fusca*; by injection as acetone-triton solutions: 1986

Insecticide	MLD In < 7 Days (µg/g)	Maximum Tolerated Dose 7 Days (µg/g)
Heptachlor	1.6	5
Chlordane	8	14
Aldrin	1.3	2.6
Isodrin	1.5	2.7
Dieldrin	1.5	2.6
Endrin	1.3	2.5
Control (acetone-triton)	454	1388

(17) Heptachlor and others vs. *Chrysops discalis*; by topical application: 2707

Insecticide	LD_{50} (estimated)(µg/fly)	LD_{90} (µg/fly)
Heptachlor	40	200
Lindane	4	35
Endrin	9	80
DDT	20	250
Dieldrin	20	950
Methoxychlor	30	90
Aldrin	40	170
EPN	48	120
Isodrin	60	170
Chlordane	60	650
Chlorothion®	65	420
Diazinon	90	360
O,O-diethyl(3-chloro-4-methylumbelliferone) thiophosphate	90	910
Q-137	120	400
Malathion	130	330
Toxaphene®	180	480

(18) Heptachlor and other substances vs. *Protoparce sexta* (5th instar); av. wgt 5.4 (4.1-7.5) g, by topical application: 1306

Insecticide	LD_{50} (µg/larva)	LD_{90} (µg/larva)
Heptachlor	1058	4005
Endrin	42	219
Parathion	52	183
Isodrin	87	490
Lindane	206	1235
Malathion	481	1276
Dieldrin	482	2559
Aldrin	487	1359
Toxaphene®	1363	5778
DDD	2622	9813
DDT	≫4000	—

(19) Heptachlor and other insecticides: Effect on *Pyrausta nubilalis* in *Zea mays* ears: 675

Insecticide	Lbs/100 Gallons	% Reduction In *P. nubilalis* Infestation By	
		Direct Action	Residual Action
Heptachlor	1.0	70	77
EPN®	.75	57	79
Aldrin	.75	70	74
DFDT	1.0	64	73
Dieldrin	.5	78	49
DDT	1.0	54	40
Parathion	.5	65	18

(20) Heptachlor and others vs. *Anasa tristis*; various routes of application: 3376

Insecticide	% Kill At 72 Hrs. At Dosages Shown					% Kill After 30 Min Exp To Surfaces Treated 7 Days Before At 100 mg/ft². % Kill In			
	32µg/g	64µg/g	128µg/g	256µg/g	512µg/g				
	Topical Application In Acetone Solution					24 hrs.	48 hrs.	72 hrs.	96 hrs.
Heptachlor	—	83.3	90	100	100	0	10	20	20
Parathion	100	100	100	100	100	10	10	20	40
Lindane	83.3	100	100	100	100	10	20	20	20

(20) Heptachlor and others vs. Anasa tristis; various routes of application: (continued) 3376

Insecticide	% Kill At 72 Hrs. At Dosages Shown Topical Application In Acetone Solution 32μg/g	64μg/g	128μg/g	256μg/g	512μg/g	% Kill After 30 Min Exp To Surfaces Treated 7 Days Before At 100 mg/ft.² % Kill In 24 hrs.	48 hrs.	72 hrs.	96 hrs.
Aldrin	—	93.3	100	100	100	0	0	0	0
Endrin	—	—	100	100	100	—	—	—	—
EPN®	—	—	100	100	100	—	—	—	—
Isodrin	—	—	90	100	100	—	—	—	—
Dieldrin	—	—	70	100	100	30	80	80	100
Chlordane	—	—	36.7	80	90	—	—	—	—
Toxaphene®	—	—	16.7	66.7	82	—	—	—	—
DDT	—	—	20	30	76.7	—	—	—	—

Rate of action at the lowest topical dosage yielding 90% mortality or better of adult Anasa tristis in 72 hours:

Insecticide	μg/g	% Kill At 12 hrs.	24 hrs.	48 hrs.	72 hrs.
Heptachlor	128	10	50	80	90
Parathion	6	3.3	33.3	76.7	90
Lindane	64	—	80	100	100
Aldrin	64	—	23.3	76.7	93.3
Endrin	128	6.7	20	86.7	100
EPN®	128	10	26.7	76.7	100
Isodrin	128	0	10	63.3	90
Dieldrin	256	0	70	96.7	100
Chlordane	512	—	6.7	73.3	90

(21) Heptachlor and other compounds vs. Musca domestica adults; applied as space sprays by the Campbell Turntable Method in kerosene sprays; 100 insects per trial: 1152

Insecticide	Conc. (mg/cc)	% "Knockdown" 25 Min.	Mean Mortality 24 Hrs. (%)	LC$_{50}$ (mg/cc)	Relative Toxicity Compared To Pyrethrins	Chlordane (Tech)
Heptachlor	0.5	14	100			
"	.25	8;4	100;93	→ 0.114±.009	28	4.0;4.4
"	.125	7;5	73;45			
"	.063	7	17			
Chlordane (tech) A	1.0	8	99	→ 0.33 ±.04	4.2	1.0
"	.5	7	74			
"	.25	11	33			
Chlordane (tech) B	1.0	9	93	→ 0.39 ±.05	3.5	1.0
"	.5	11	70			
"	.25	6	20			
Chlordane (tech) A	1.0	10	84	→ 0.52 ±.039	6.4	1.0
"	.5	3	51			
"	.25	6	12			
Chlordane crystalline	1.0	9	66	→ 0.743±.055	4.5	.7
"	.5	9	28			
"	.25	6	11			
Aldrin	.25	7;5	85;82	0.131±.01	25	4.0
"	.125	8;6	45;51	0.129±.017	22	4.0
"	.063	9;3	15;15			
Dieldrin	.25	5	98	→ 0.088±.011	32	5.9
"	.125	1	74			
"	.063	2	27			
Pyrethrins	8.0	100	82	→ 1.37 ±.016 3.32 ±.025 2.83 ±.36	1.0	
"	4.0	100;100	58;63			
"	2.0	100;100;100	71;26;36			
"	1.0	100;100;100	32;13;17			

The differences in the various values reflect variations of resistance and susceptibility of different fly "populations".

c) Heptachlor and beneficial insects:

(1) Vs. Apis mellifera: Heptachlor is considered highly hazardous for bees foraging on treated blooming plants. For details of toxicity for honeybees, consult the section in this work titled Bees and Insecticides. 131

(2) Treatment of certain crops with heptachlor has been followed by resurgences of *Tetranychus pacificus* due to destruction of natural predators. 2650

(3) Laboratory effects of heptachlor and others as dusts on three beneficial insects; tested in cage tests by placing adult insects on plants previously treated by the vacuum dusting method: 1404

Insecticide & Conc. In Dust		% Mortality 24 Hrs. Of		
		Collops vittatus	*Hippodamia convergens*	*Coleomegilla maculata*
Heptachlor	2.5%	41	30	38
DDT	5.0%	38	6	32
Perthane	5.0%	23	6	12
Strobane	5.0%	10	18	12
Toxaphene®	10.0%	32	12	36
Endrin	1.0%	27	10	18
Dieldrin	2.0%	36	4	24
Parathion	2.0%	65	78	98
Malathion	5.0%	47	90	100
Chlorothion®	5.0%	64	82	100
Diazinon	4.0%	37	66	100
Control	0	11	4	0
Lowest Sig. Difference (5% level)		20	24	26

d) Pharmacological, pharmacodynamical, physiological, etc.; insects:

(1) Data, specifically related to the mode of action and pharmacodynamical properties of heptachlor 333,1170
in insects, are so meager as to be virtually non-existent. Since this is true of the "cyclodiene 353,2231
insecticides" generally, little inference can be drawn from analogy. The toxicological studies 2093, 642
indicate the great role played by structure in the modification and "nuancing" of toxicity and 2643,2639
thus, presumably, of action, rate of action, etc. in the intoxicated or treated insect. 2638,2645, 722

(2) Heptachlor (like the others of its group) elicits, after a latent period of 3 hrs. approximately, trains of spontaneous, repetitive discharges from the crural nerve of *Periplaneta americana*. 520

(3) With heptachlor (as with others of its group) the immediate rise in O_2 consumption noted with such toxicants as DDT, methoxychlor, lindane, TEPP, p-dichlorobenzene, pyrethrins, nicotine, dinitro-compounds, azobenzene, is preceded by a latent period during which the intoxicated insect is passive. The rise in O_2 consumption is correlated with the period of spontaneous nerve discharges. Thus, $10\mu g$ by injection of heptachlor to *Periplaneta americana* was followed, after a latent period relatively brief, by an increase in O_2 consumption from 0.6 mm³/minute/insect to ca. 1.6 mm³/minute/insect in 200 minutes. 1441

Rate of O_2 Consumption in *Blattella germanica* following $10\mu g$/insect of various insecticides given by injection: 1441

Heptachlor	Latent Period Brief	O_2 ↑ from ca. .6 mm³/min/insect to ca. 1.6 mm³/min/insect at 200 min.
β-Chlordane	Latent Period > 200 min	O_2 ↑ from ca. .8 mm³/min/insect to ca. 4 mm³/min/insect at 250 min.
Aldrin	Latent Period ca. 200 min	O_2 ↑ from ca. .5 mm³/min/insect to ca. 3 mm³/min/insect at ca. 250 min.
Dieldrin	Latent Period ca. 100 min	O_2 ↑ from ca. .7 mm³/min/insect to ca. 3.5 mm³/min/insect at ca. 200 min.

(4) In *Musca domestica* (as in dogs, rats) heptachlor is converted to the epoxide of heptachlor. It has been 709
suggested that the epoxide, the product of metabolic degradation, may be the really active toxic prin- 1597,710
ciple.

(5) Heptachlor (along with the other chlorinated hydrocarbons tested) at a concentration of 10^{-3} M gave complete inhibition of coxal muscle cytochrome oxidase of *Periplaneta americana* ♂ as measured by O_2 uptake in the Warburg apparatus; at 10^{-5} M occurred a slight, transient stimulation. The inhibition is rapid in onset with heptachlor. 2305

(6) The question of dechlorination in the body as the mechanism of toxic action, as has been proposed, is 2231
not supported by heptachlor which, while the most effective insecticidally of the chlordane series, is 2123
resistant to dechlorination, and much more so than enneachlor and β-chlordane, which are less insecticidal than heptachlor.

e) Heptachlor in the economic control of insects; reports of field experiences:

(1) Vs. *Paratetranychus citri*: Virtually ineffective as a residual treatment; as a direct spray (as a 1% solution) 56% kill was obtained in 24 hrs. (0% with DDT, 50% with lindane). 2692

(2) Inferior to DDT in the airplane spray control of *Pyrausta nubilalis*. 105, 106

(3) Vs. corn rootworm: Heptachlor (with aldrin and BHC) is one of the leading present day insecticides, being effective at low dosages. 1998

(4) Vs. wireworms: Superior to chlordane which is 4 times less effective than lindane. 2583

(5) Vs. *Cyclocephala* sp: Superior to aldrin, parathion and others. 2519

(6) Vs. *Aëdes* spp. larvae: In rank of effectiveness—Parathion > DDT, DDD, methoxychlor > heptachlor 764,2168
> chlordane > toxaphene > BHC. 3114

(7) Vs. *Aëdes aegypti* (larva): 0.016 ppm ⟶ 100% kill. 1427

(8) Vs. *Periplaneta americana*, *Blattella germanica*: Slightly less toxic than dieldrin, slightly > toxic than aldrin, lindane; 5 times as toxic as chlordane by topical application. 1757

(9) Vs. *Melanoplus femur-rubrum*: Effective control obtained at 2-4 oz per acre; slightly < residual power than aldrin.

(10) Vs. *Melanoplus differentialis*: As in preceding.

(11) Vs. *grasshoppers*: At 0.1 lb/acre (emulsions) gave control = to dieldrin (80-90% kills) in range grass; residual action for 1-3 weeks. In dry baits at 0.1 lb/100 lb gave = control with aldrin at same dosage, toxaphene at 1 lb/100 lb, chlordane at 0.5 lb/100 lb. 2445

(12) Vs. *Thrips tabaci*: 0.5 lb per acre gave control. 2148

(13) Vs. *Blissus leucopterus* (adult): Inferior to DNOC. 1757

(14) Vs. *Tetranychus bimaculatus*: Inferior toxicant action. 1772

(15) Vs. *Aphis fabae*: In comparison with 44 other insecticides "poor" in action; complete control only at >1 lb per 100 gallons. 1772

(16) Vs. *Epilachna varivestis*: "Poor" in control action. 1772

(17) Vs. *wireworms*: At 2-4 lbs per acre gave economic control of heavy infestations on potato crops. 2583

(18) Vs. *Popillia japonica*, *Cyclocephala borealis*: At 1 lb per acre gave effective control with somewhat higher kills of *Cyclocephala* than those obtained with aldrin, parathion, BHC, DDT, chlordane, toxaphene, lead arsenate. 2643

(19) Vs. *Cortinus nitida* larvae in soil: At 4 lbs per 100 yds^2 < effective than lindane at 2 lbs, or parathion at 1 lb. 822

(20) Vs. *Conotrachelus nenuphar*: As a spray = in effectiveness initially and residually to aldrin; superior to DDT, toxaphene, chlordane; inferior to lindane. 1757

(21) Vs. *Attagenus piceus*: Initial toxicity very high; less effective residually than DDT. 1757

(22) Vs. *Pyrausta nubilalis* in corn: Ineffective at 0.5 lb/acre. 106

(23) Vs. *Carpocapsa pomonella*: Essentially ineffective; far < effective than DDT, lindane, parathion. 1757

(24) Vs. *Prodenia eridania*: Excellent control; complete kills at < 0.0625 lb/per 100 gallons water. 1772

(25) Vs. *Stomoxys calcitrans*: Very slow "knockdown" compared with DDT, methoxychlor; also < persistent residually. 921

(26) Vs. *Hylemyia antiqua*: As a dust in seed furrows at planting gave control. 2584

(27) Vs. *Melophagus ovinus*: = to dieldrin, aldrin, lindane; < effective than parathion; > effective than DDT, DDD, methoxychlor, chlordane, toxaphene, rotenone. 353

f) *Screening test data*:

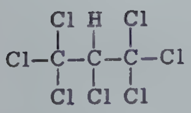
(1) For screening test data vs. *Pediculus humanus corporis*, *Xenopsylla cheopis*, *Ctenocephalides felis*, *Amblyomma americanum*, *Musca domestica*, various mosquitoes, *Blattella germanica* consult Ref. 1801.

g) *Phytotoxicity*:

(1) As a soil insecticide, used at 50 lb per acre, no important adverse effects were registered for field corn or soy beans. 1996

97

HEPTACHLOROPROPANE



$Cl_3C{-}CHCl{-}CCl_3$

Molecular weight: 285

GENERAL

A low vapor pressure fumigant which, as a spot fumigant, surpasses in long lasting effectiveness trichloroacetonitrile, acrylonitrile, chloroacrylonitrile, trichlorobutyronitrile. 2853

PHYSICAL, CHEMICAL

A liquid; m.p. ca. 11°C; b.p. 240°C; specific gravity 1.8; v.p. 0.09 mm Hg at 25°C; vapor saturation in air at 25°C = 1.4 mg/l; virtually insoluble in water; soluble in most organic solvents. 353

TOXICOLOGICAL

Toxicity for higher animals: No data are available to this compilation at the time of preparation.

Toxicity for insects:

1) Comparative toxicity for *Tribolium confusum* (adult) of symmetrical and asymmetrical heptachloropropane and certain other halogenated aliphatic hydrocarbons. Exposure 5 hours, at 25°C, empty vessel fumigation: 353

Fumigant	LC_{50} (mg/l)
sym.-Heptachloropropane	2.5
asym.-Heptachloropropane	4.1
Hexachloropropene	1.1
2,3-Dichloropropene-1	2.9
Hexachlorobutadiene	4.0
1,3-Dichloropropane	10
1,4-Dichlorobutane	11
Isocrotyl chloride	12
Ethylene dichloride	19
Propylene dichloride	40
1,1,1-Trichloroethane	66
Dichloromethane	82
Trichloroethylene	108
Chloroform	157
Carbon tetrachloride	185
Allyl bromide	9
Methyl bromide	11
Isocrotyl bromide	14
Ethylene dibromide	14
Butyl bromide	100
Ethyl bromide	150

2) Residual action: Duration of the toxic effect of sym.-heptachloropropane and some other low vapor pressure fumigants in open vessels of flour: Test insect: *Tribolium confusum* (adult). 375 g flour 3 inches in depth exposed to 2 ml of each fumigant on impregnated blotting paper, separated by gauze from the exposed flour. Insects exposed below and near the surface of the flour. Exposures of insects 4 days; mortality assessed 3 days after end of exposure: 2853

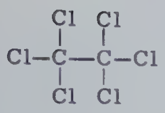
Fumigant	V.P. mm Hg At 25°C	Time During Which The Given % Mortality May Be Had	
		50-100% (days)	100% (days)
sym.-Heptachloropropane	0.1	176	112*
Acrylonitrile	117.0	2	1
Chloropicrin	24.0	2	2
Ethylene dibromide	13.5	20	12
Dichloroethyl ether	3.0	28	0
Hexachloropropene	0.3	172	66
Lindane (as 40% acetone solution)	2.1×10^{-5}	0	0**

*Still 100% effective at end of experiment.

**Test terminated at 50 days.

98

HEXACHLOROETHANE (1, 1, 1, 2, 2, 2-Hexachloroethane; Carbon hexachloride)



$\mathrm{Cl{-}\overset{Cl}{\underset{Cl}{C}}{-}\overset{Cl}{\underset{Cl}{C}}{-}Cl}$

Molecular weight: 236.76

GENERAL

[Refs.: 177, 2289]

A substance which has been proposed for certain special uses in the control of insects. Formulated as tablets (hexachloroethane 10% in starch) use has been made of this compound to control *Heliothis armigera* in corn, the tablets being inserted manually in the tip of the developing ear of *Zea mays*. Reported to be effective in control of clothes moth. Employed in treatment of the psoroptic mange of cattle and horses. Used also as a veterinary anthelmintic.

PHYSICAL, CHEMICAL

A crystalline solid (rhombic crystals) at room temperature; b.p. 184.4°C; m.p. 186.9-187.4°C (sealed tube); $d_4^{20°}$ 2.091; soluble in water to 0.005 part in 100 parts at 22°C; readily soluble in alcohol and ether. 3199

TOXICOLOGICAL

1) Toxicity for higher animals: 3199
   a) Acute toxicity:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Dog	iv	LD_{30} min.	325	In oil solution; death in 30 minutes.	195

(1) Oral doses, 13.5 g and higher, are reported to induce toxic effects in sheep, with the following signs: Inability to rise; central depression to varying degrees; staggering walk; fine tremors in muscles of lips, face, neck, forelegs; weak, but slightly accelerated pulse; shallow, but otherwise normal breathing. 3199

(2) Dogs, following oral doses, revealed gastro-intestinal irritation; renal irritation reported after anthelmintic administration. No evidence, in dogs, of liver damage following repeated oral and subcutaneous administration.

(3) Less toxic for the dog than pentachloroethane (LD, iv, 100 mg/k) or chloroform (LD, iv, 90 mg/k).

(4) Turbidity of the cornea, in dogs, has been reported not to attend inhalation or topical administration to the eye of hexachloroethane.

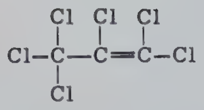
(5) No information on toxicity for man. Inhalation hazard is moderate in view of the high boiling point and low volatility. Cutaneous absorption may be viewed as a potential hazard.

Pharmacological, pharmacodynamic, physiological, etc.: 3199

1) Absorption into the body via gastro-intestinal route, and, moderately, by the pulmonary portal, has been shown, as has cutaneous absorption to a fatal amount, via the skin of rabbits.
2) Metabolic fate and excretion remain virtually unknown; reducing substances in the urine, as have been shown following intake of other chlorinated hydrocarbons, have not been detected by one investigator in the case of hexachloroethane.
3) Possesses modest narcotic properties. 1 to 1.4 mg/k in dogs have caused moderate CNS depression, staggering walk, muscle weakness and twitching. Rabbits have shown, on inhalation of the vapors, a slow, progressive CNS depression.
4) On the nerves of arthropods (isolated *in vitro*), hexachloroethane is stated to show a reversible, DDT-like effect. 3278
5) Bactericidal to the *Vibrio* of Metchnikov at 0.00002243 mole/l, 24 hours contact, being more effective, in this respect, than pentachloroethane which kills *Vibrio* at 0.00064 mole/l, 24 hours contact. 3199

99

HEXACHLOROPROPENE



$\mathrm{Cl{-}CCl_2{-}CCl{=}CCl{-}Cl}$

Molecular weight: 249

GENERAL

[Refs.: 353, 2853]

A slowly volatile, long-lasting, persistent fumigant insecticide, suitable for the protection and disinfestation of dead spots in flour mills, cereal processing plants, storage places, etc. Useful in protecting granaries from such stored products insects as Sitophilus, Tribolium, Ephestia, Plodia, Sitotraga, Oryzaephilus, Rhizopertha and others. Surpasses in long-lasting effectiveness the various alkyl and aryl nitriles.

PHYSICAL, CHEMICAL

A pale, yellow liquid which becomes darker with time; m. p. $<0°C$; b.p. 208°-212°C; $d_{20^\circ}^{20^\circ}$ 1.7; v.p. 0.3 mm Hg at 25°C, 17.3 ± 5% mm Hg at 99°C; virtually insoluble in water; soluble in most organic solvents; corrosive to copper, solder alloy, paints, varnishes, natural and artificial rubber, "lucite", "plexiglas". Vapor saturation at 25°C = 6.6 mg/l. 2940 353

TOXICOLOGICAL

1) Toxicity for higher animals: 2940,3199

Animal	Route	Dose	Dosage	Remarks	
Rat	ip	LD_{50}	ca. 0.4 mg/k	Hepatic damage in 24-48 hrs.	2940,3199
Rat	inh	LC_{50}	425 ppm	30 minutes exposure; death in 2-14 days.	2940,3199
Mouse	inh	LC_{50}	530 ppm	30 minutes exp.; death in 1 day.	2940,3199
Rabbit	inh	MLD(ca.)	85 ppm	30 minutes exposure.	2940,3199
Rabbit	inh	LC_{100}	310 ppm	30 minutes exposure; death in 6-7 days.	2940

a) Hexachloropropene lacks narcotic action on exposed animals.
b) Exposure to the vapor leads to marked nervous stimulation and excitement.
c) The principal overt sign of intoxication is respiratory difficulty with gasping and difficulty in inhalation and expiration.
d) Blood tinged discharges from the nose and in the respiratory tree may persist after exposure.
e) Delayed effects have been noted in exposed animals. Rats and rabbits have relapsed from a week to 12 days after exposure, with death ensuing for 1/5th of the subjects.
f) Rabbits are reported to be more sensitive than rats or mice.
g) Exposed cats revealed a critical time of two days with most subjects (in this case 97%) dead in 24 hrs, and all dead in 48 hrs.
h) Anhydremia and highly concentrated urine noted in exposed rats.

2) Sub-chronic toxicity; repeated exposure: 2940,3199
a) Rabbits exposed 6 hrs per day, 5 days per week to 50 ppm (approx.) concentrations, (2 subjects) showed: Death of one animal after 13 days exposure, survival and recovery of one animal subjected to a like exposure.
b) Amounts of hexachloropropene as low as 0.0005 cc produced erythema and irritation, of the skin of test rabbits.

3) Pathology: 3199
a) Principal pathological findings at autopsy of exposed animals are: Lung engorgement, oedema, hemorrhage, atelectases, local areas of pneumonia (infrequent). About 1/3rd of the subjects revealed hepatic necrosis, primarily periportal in site.
b) Rats, which survived intraperitoneal injections of the LD_{50} dosage, showed fatty deposits in the liver lobules, centrally; epithelial proliferation in the bile ducts of the portal area with replacement of necrotic cells.
c) Periportal and peripheral hepatic necrosis was apparent in from 24-48 hours among rats receiving the intraperitoneal LD_{50} dosage.

4) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Ephestia kühniella	Fumig	LC_{50}	4 ppm		353
Sitophilus granarius	Fumig	LC_{50}	450 ppm		353
Tribolium confusum	Fumig	LC_{50}	10 ppm		353
Tribolium confusum	Fumig	LC_{50}	1.1 mg/l	Exposure 5 hrs at 25°C, empty vessel.	353

(1) Comparative toxicity of hexachloropropene and other aliphatic hydrocarbon fumigants for Tribolium confusum (adult) exposed for 5 hours at 25°C to empty vessel fumigation: 353

Fumigant	LC_{50} (mg/l)
Hexachloropropene	1.1
sym.-Heptachloropropane	2.5
2,3-Dichloropropene-1	2.9
Hexachlorobutadiene	4.0
asym.-Heptachloropropane	4.1
1,3-Dichloropropane	10
1,4-Dichlorobutane	11
Isocrotyl chloride	12
Ethylene dichloride	19
Propylene dichloride	40
1,1,1-Trichloroethane	66
Dichloromethane	82
Trichloroethylene	108
Chloroform	157
Carbon tetrachloride	185
Allyl bromide	9
Methyl bromide	11
Isocrotyl bromide	14
Ethylene dibromide	14
Butyl bromide	100
Ethyl bromide	150

(2) A tabulation comparing the residual effect of several low vapor pressure fumigants in flour, among them hexachloropropene, may be found in this work under the title, Heptachloropropane.

100

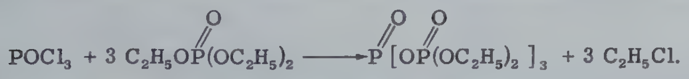
"HEXAETHYL TETRAPHOSPHATE" (Bladan; HETP.)

(Also consult Tetraethyl pyrophosphate, TEPP)

GENERAL

[Refs.: 2769, 2775, 3369, 345]

Hexaethyl tetraphosphate was the name applied to a product identified with the empirical formula $C_{12}H_{30}O_{13}P_4$, of an apparent molecular weight of 506.3. The substance was described as the result of the following reaction:



$$POCl_3 + 3\ C_2H_5O\overset{O}{P}(OC_2H_5)_2 \longrightarrow P\,[O\overset{O}{P}(OC_2H_5)_2\,]_3 + 3\ C_2H_5Cl.$$

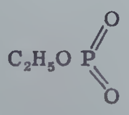
A similar product has been described (and patented) which was the outcome of the following reaction:

$$2\ (C_2H_5O)_3\,P = O + P_2O_5 \longrightarrow (C_2H_5O)_6\ P_4O_4\,.$$

The product was generally characterized as having the following physical and chemical properties: 345,353,2231,2128

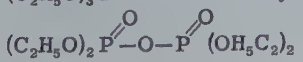
A light-amber, oily liquid; freezing point ca. -40°C; $d_{4^\circ}^{27^\circ}$ 1.2917, $d_{4^\circ}^{25^\circ}$ 1.271; $n_D^{27^\circ}$ 1.427; decomposes on heating to 190°C (according to some) 145°C-150°C (according to others) with the liberation of ethylene; miscible with water, alcohol, acetone, ether diacetone alcohol, ethyl acetate, glycerol, chloroform, chlorobenzene, carbon tetrachloride, benzene, toluene, xylene, alkyl naphthalenes; insoluble in kerosene, ligroin; ready hydrolysis in water; corrosive in the presence of water to some metals, for example, a 0.1% solution (pH 2.45) was not corrosive to iron, brass after 106 hours at 25°C-30°C; 1.0% solution (pH 1.54) not corrosive to brass after 106 hours at 25°-30°C; galvanized iron rapidly attacked after 4 hours, at 30°C, at which time 60% of "galvanize" was removed. Originally marketed as a 60% emulsion in 20% toluene + 20% emulsifying agent as "Bladan". 554,555 1341, 314 1382

Actually, the two reactions shown above are now known to yield an undistillable mixture of linear polyphosphates including:



ethyl metaphosphate

$(C_2H_5O)_3\,P = O$ triethyl phosphate



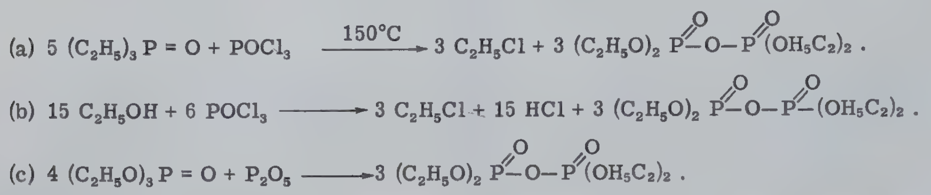
$$(C_2H_5O)_2\overset{O}{P}{-}O{-}\overset{O}{P}(OH_5C_2)_2$$

tetraethyl pyrophosphate (TEPP)

and possibly pentaethyl triphosphate. A. W. A. Brown [353] quoting H. Coates [554,555] speaks of the presence of "linear hexaethyl tetraphosphate." Bowen and Hall [314] refer to "the so-called hexaethyl tetraphosphate," evidently acknowledging that such a material does not exist as a product of the above reactions even in the resulting mixture.

Tetraethyl pyrophosphate, which is now viewed as the truly insecticidally active principle of what was called HETP (Bladan) is found in the yields of the first reaction in amounts of 20%-40%, depending on the molar ratio of the reagents triethyl phosphate and phosphorus oxychloride (3:1 or 5:1). It is the product with the lower yield of tetraethyl pyrophosphate which has been called HETP, while that with the higher yield is called TEPP.

Metcalf [2231] summarizes the various processes leading to the formation of tetraethyl pyrophosphate as follows:



(a) $5\ (C_2H_5)_3\,P = O + POCl_3 \xrightarrow{150°C} 3\ C_2H_5Cl + 3\ (C_2H_5O)_2\,\overset{O}{\overset{\|}{P}}{-}O{-}\overset{O}{\overset{\|}{P}}(OH_5C_2)_2\,.$

(b) $15\ C_2H_5OH + 6\ POCl_3 \longrightarrow 3\ C_2H_5Cl + 15\ HCl + 3\ (C_2H_5O)_2\,\overset{O}{\overset{\|}{P}}{-}O{-}\overset{O}{\overset{\|}{P}}{-}(OH_5C_2)_2\,.$

(c) $4\ (C_2H_5O)_3\,P = O + P_2O_5 \longrightarrow 3\ (C_2H_5O)_2\,\overset{O}{\overset{\|}{P}}{-}O{-}\overset{O}{\overset{\|}{P}}(OH_5C_2)_2\,.$

The mixture, which has been called hexaethyl tetraphosphate (HETP), readily hydrolyzes, yielding a mixture of mono- and diethyl-phosphoric acids. Pure tetraethyl pyrophosphate hydrolyzes to yield diethyl phosphoric acid as a reaction of the first order.

TEPP is much more toxic than the mixture called HETP and is the active constituent of the latter.

However, since data appear in the "literature" on the toxicity of HETP as such, these are included here. They must be interpreted with the foregoing remarks in mind.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) HETP was, from the beginning, described as hazardous, extremely toxic, and rapid in its intoxicating action. Readily absorbed via the skin with but slight irritation, the danger level for repeated inunction being 5 mg/k. Cumulative toxicity was reported as possible. Maximum protection for formulators, handlers, spraymen, etc. was recognized as *de rigueur*. Atropine was recognized as the antidote. 1949, 724 2868
   b) Acute toxicity; higher animals:

Animal	Route	Dose	Dosage (mg/k)	
Mouse	or	LD_{50}	55.5	1332
Mouse	sc	LD_{50}	0.9	1051
Mouse	ip	LD_{50}	6.1	724
Rat	or	LD_{50}	1.9	1051
Rat	or	LD_{50}	7.0	1332
Rat	sc	LD_{50}	0.7	1051
Rat	ct	LD_{50}	25.0	1051
Guinea Pig	or	LD_{50}	16.0	1332
Guinea Pig	sc	LD_{50}	2.2	1051
Guinea Pig	ct	LD_{50}	120.0	1051
Rabbit	or	LD_{50}	20.5	1332
Rabbit	iv	LD_{50}	0.69	1332
Rabbit	ct	LD	0.06 cc/k*	744
Dog	im	LD	ca 1.5	724
Dog	iv	LD	ca 1.3	724

* As a 2.5% aqueous solution.

   c) Pharmacological, pharmacodynamical, physiological, etc.; higher animals: 852
      (1) A potent inhibitor of mammalian nerve and brain choline esterase, *in vitro* and *in vivo*. 724,864, 852
      (2) Administration is followed by rapid evolution of muscarinic and nicotinic, signs. 724, 864
      (3) In dogs, cats; symptoms of intoxication: Salivation, vomiting, involuntary defecation, urination, tremors leading to prostration, opisthotonus, convulsions, followed by death in respiratory failure from heavy bronchial secretions and constriction. 724, 864 852
      (4) In man: Symptoms include: Headache, chest tightness, breathing difficulties, extreme contraction of pupils with visual derangement (an ominous sign). 3255
      (5) Effects of sub-acute and sub-lethal doses may require several days to pass away; necrosis of gall bladder is remarked as a possible sequel. 1949
      (6) It is evident that the symptoms are those of intense cholinergic overstimulation in accord with the powerful choline esterase inhibitory properties of HETP. All the above effects are produced equally by TEPP. 852
   d) Phytotoxicity:
      (1) Phytotoxic hazard, in general, considered slight.
      (2) Of 130 species of plants (greenhouse tests), tomato plants and some Chrysanthemum varieties were damaged by 10% aerosols at 10 g per 1000 ft^3. Signs included: Black, necrotic spots, "scorching." Roses and carnations proved sensitive under conditions of bright sun. 2875

(3) With 0.1% sprays (greater than insecticidal concentrations) tomatoes were "scorched." With >0.05% soil drenches tomatoes were killed. With thermal vapors tomatoes showed "cooked" leaves, stem effects epinasty. 3399

(4) Pear, peach, plum foliage may show damage as small, perforating necrotic spots; damage enhanced by high temperatures and humidity. 2524,2743 84

(5) May increase yield of potatoes and benefit corn (nutritional factor?). 3355

e) Toxicity for insects:

(1) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Apis mellifera (worker adult)	or	LD_{50}	0.29 µg/bee	Parathion 0.75µg/bee, TEPP 0.07µg/bee.	910
Melanoplus differentialis (adult)	Topical	LD_{50}	18.4 µg/g	TEPP 4.4 µg/g.	3267
Musca domestica (adult)	Contact Spray	LC_{50}	0.52 ± .05 mg/cc	Kerosene + acetone (1:1) sprays.	1164

2) Comparative toxicity HETP and other compounds:

a) Vs. Musca domestica (adult) as acetone + kerosene (1:1) contact sprays: 1164

Insecticide	Conc. (mg/cc)	Mean Mortality (24 hr)(%)	Mean Conc. For 50% Kill (mg/cc)	Relative Toxicity
HETP	0.64	58	0.52 ± .05	1.0 (standard)
"	.32	33		
"	.16	3		
TEPP	.3	100	0.095 ± .01	5.5 ± .07
"	.15	70		
"	.074	43		
"	.037	10		
Parathion	.079	100	0.03 ± .003	17.0 ± 2.0
"	.039	71		
"	.026	47		
"	.020	11		
Pyrethrins	2.0	70	1.2 ± .14	0.43 ± .06
"	1.0	45		

b) Vs. Melanoplus differentialis (adults), by topical application as dioxane acetone, or ethanol solutions: 3267

Insecticide	LD_{50} Topical (µg/g)
HETP	18.4
TEPP	4.4
Parathion	0.7; 0.8
Dieldrin	1.4
Aldrin	1.8
Heptachlor	2.6; 1.6
Lindane	1.6; 3.4
Chlordane	16.3; 9.8
Toxaphene®	73.9; 61.0
DDT	9380.0

c) Vs. 3 species of aphids: 899

Insecticide 0.05% conc.	Brachycaudis helichrysi (Insects/100 leaves)		Phorodon humuli (Insects/100 leaves)		Aphis pomi (Colonies/Plot)		
	Before Spray	After Spray	Before Spray	After Spray	Before Spray	7 Days After	24 Days After
HETP	2132	40	3120	53	36.0	2.8	20.2
Parathion	1445	10	2580	5	35.8	5.0	14.4
Nicotine	1881	250	2630	422	18.4	5.0	17.4
Control	2467	3260	2740	2267	25.8	32.8	22.4

d) Vs. overwintering eggs of Aphis pomi and Operophtera brumata; mortality tested by dipping eggs for 10 seconds in given insecticide concentrations 100 to >300 eggs per trial: 899

Compound	% Mortality At Concentrations Of			
	A. pomi		O. brumata	
	0.2%	0.05%	0.2%	0.05%
HETP	7.4	1.1	6.2	3.7
Triethyl phosphate	1.4	0	3.1	7.1
Triphenyl phosphate	14.1	0	8.0	6.4
Tri-o-tolyl phosphate	0	7.1	5.8	7.9
Triphenyl phosphine	13.9	5.1	3.4	3.6
Parathion	100	78.6	95.4	90.8
Diethyl acetyl phosphate	5.7	8.4	8.7	1.3
p-Nitrophenyl diethyl phosphate	99.6	100	7.8	4.4
Diphenyl ethyl thionophosphate	0	8.1	8.5	4.8

d) Vs. overwintering eggs of Aphis pomi and *Operophtera brumata*; mortality tested by dipping eggs for 10 seconds in given insecticide concentrations 100 to > 300 eggs per trail: (continued) 899

Compound	% Mortality At Concentrations Of			
	0.2%	0.05%	0.2%	0.05%
	A. pomi		*O. brumata*	
p-Nitrophenyl dichlorothionphosphonite	40.4	10.3	—	10.2
Diphenyl chlorothionphosphonate	25.9	4.9	4.0	3.0
Tri-(p-nitrophenyl) thionophosphate	5.3	0.6	1.9	4.3
Tri-(p-chlorophenyl) thionphosphate	15.7	13.0	1.6	1.9
TEPP	3.3	2.6	7.2	6.5
Diethyl 1-carbethoxyprop-1-en-2yl phosphate	100	86.3	18.3	2.3
Phenyl diethyl phosphate	59.3	2.9	2.5	3.3
p-Chlorophenyl diethyl phosphate	93.9	14.6	2.5	2.2
Phenyl diethyl thionphosphate	39.9	3.7	1.7	1.6
Triphenyl thionphosphate	19.0	23.7	0	3.7
Tetraethyl dithionophosphate	100	54.6	24.0	4.6
Tetraethyl monothionophosphate	12.0	2.4	19.0	1.6
Pyrophosphoric tetrakis dimethylamide	9.0	0	1.4	0
Control hatch	69.9		97.1	

e) Toxicity for beneficial insects:
   (1) Exceedingly toxic for *Apis mellifera*. Contact toxicity is high, but there is no residual effect. 909,910,927,429
   (2) Consult the section in this work titled, Bees and Insecticides.

f) Resistance to HETP:
   (1) Acaricide resistant "populations" of two-spotted spider mites have appeared in a few greenhouses and become widely distributed. HETP, as an aerosol in methyl chloride, at concentrations which gave 99.7% kills of the non-resistant strains, yielded but 39% kills of the resistant types. 2867

3) Pharmacological, pharmacodynamical, physiological, etc.; insects:
   a) Classified as a "neurotoxic poison." 2600
   b) Applied topically to *Periplaneta americana*: ↑ irritability leading to violent tremors of entire body followed by paralysis and death. 2683,2684
   c) Toxic effect manifested at the synapses of afferent and conducting nerves in the ganglia. Conduction facilitated with a ↑ in stimulation threshold. This last effect alternates with transmission blockage. Increasing concentration of the toxicant or added acetylcholine produced a continuous conduction block. 2683,2684

4) Economic control of insects with; reports of field and other experiences:
   a) Vs. *Chlorochora sayi*: Moderately toxic. 353
   b) Vs. *Cicada septemdecem*: 0.15% sprays gave 90% control on orchard trees. 676
   c) Vs. *Philaenus leucophthalmus*: Ineffective. 511
   d) Vs. *Psylla pyricola*: Less effective than parathion in control of. 2368
   e) Vs. *Trialeurodes vaporariorum*: Ready control by aerosols of HETP. 353
   f) Vs. *Brevicoryne brassicae*: 5% dusts and 0.1% sprays reported to eliminate. 346
   g) Vs. Greenhouse aphids (all spp.): Aerosols at 1 mg per ft^3 gave complete control. 2868,2872,2873,2875
   h) Vs. *Myzus persicae*: On celery, superior to DDT in control of. 1137
   i) Vs. *Myzus porosus*: On roses, sprays at 1 to 5000 concentration gave 90% kills. 2053
   j) Vs. *Pentalonia* spp: On banana plants proved no more effective than nicotine. 2906
   k) Vs. *Eriosoma lanigerum*: Gave effective control of. 2368

101

HYDROGEN CYANIDE (Hydrocyanic acid; Hydrocyanic acid gas. As an aqueous solution: Prussic acid.)

H — C ≡ N   Molecular weight 27.03

GENERAL

(Also consult the general treatment titled, Fumigants, in this work)
[Refs.: 2815,353,1059,757,2120,539,129,1925,1221,605,1828,436,611,3261,2002,155,606,2323,1916]

An exceedingly poisonous gas which, in spite of the toxicity hazard involved, is very widely used. HCN is probably the most generally toxic insect fumigant. Intensely toxic to mammals and other warm blooded forms as well as to virtually all animal and plant life. Concentrations of 200 ppm in air are fatal to man (the gas is used as an instrument of capital execution), and the most exacting precautions in its handling and use are de rigueur. As a toxicant, HCN acts with extreme rapidity, poisoning, reversibly, the enzyme systems of cellular respiration which are aerobic and make use of oxygen.

Under highly controlled conditions, to minimize the phytotoxic hazard, HCN, generated on the spot from its alkali or alkaline earth salts or released from cylinders in which it has been liquified under pressure, is used almost universally in the fumigation of citrus trees to control scale insects. In addition, HCN is used to fumigate plants in glass houses, as a house, warehouse, shiphold, boxcar, storage place, stored products and, under certain circumstances, as a fresh fruit and vegetable fumigant. In certain materials the absorption coefficient of HCN is very high. This last involves a double disadvantage, namely, low penetration into some materials, for instance stocked grains, except at very high concentrations or under pressure, and the necessity for prolonged airing of many fumigated articles, for example mattresses, upholstered furniture, houses, bedding, etc. Vacuum fumigation with HCN has been found practical and very effective.

PHYSICAL, CHEMICAL

A colorless gas at >26°C (ordinary room temperatures and above); odor like bitter almonds, but not strong enough to render the gas self-warning before hazardous levels are reached; inflammable, burning in air with a blue flame and without toxic combustion products (elimination by burning is a satisfactory method of handling liquid HCN spills under appropriate circumstances); non-explosive in the normal fumigant concentrations; freezing point < -14°C, 10°F; m.p. -14°C; b.p. 26°C; $d_{4^\circ}^{20^\circ}$ (liquid HCN) 0.688; density of gas (air = 1) 0.94; v.p. 739 mmHg at 25°C, 7610 mmHg at 20°C; vapor saturation in air at 25°C = 1140 mg/l; 1 mg/l = 906 ppm; 1 ppm = 0.001104 mg/l; very soluble in water, yielding weakly acid solutions; soluble in alcohol and ether; lower limit of flammability in air = 5.6%; bulk density: 659 cc = 1 pound, 5.7 lb = 1 gallon; 56 lb per 1000 ft^3 = maximum which can exist as a vapor in air at 68°F. Freezes to a snowy solid $\frac{7}{10}$ths the density of water; volatilizes rapidly at all temperatures to a colorless vapor, diffusing rapidly and completely in air; corrosive effect very slight, not corrosive to clothing; stable when pure; commercial preparation, 96-98% pure, is slightly acid.

a) Formulations: May be made on site by action of mineral acids on KCN and NaCN "eggs" or crystals or by action of moisture on $Ca(CN)_2$ (Cyanogas); as liquid HCN in cylinders under pressure, with 5-10% lachrymating substances added for warning purposes; absorbed on fiber discs from which the vapors are released on standing; on absorbents such as diatomaceous earth and felt for distribution in the space to be treated.

b) Maximum amounts of HCN which may exist as a vapor in a 1000 ft^3 fumigating chamber at various temperatures: 2671

Temperature (°F)	V.P. (mmHg)	Lbs As Vapor/1000 ft^3
32	264	26
59	500	47
68	610	56
77	739	67
86	760	68
95	760	67
104	760	66
113	760	65
122	760	64

TOXICOLOGICAL

a) General

(1) For man the average fatal dose = 50-60 mg; 200 ppm bring quick death; exposure to 150 ppm for $\frac{1}{2}$ - 1 hour may endanger life. 2221,1221

(2) Allowable working concentration (New Jersey, Massachusetts) 20 ppm; maximum allowable concentra- 1665
tion 10 ppm; maximum tolerated concentration (based on Guinea Pigs, and implying tolerability without 2221
serious symptoms; slight symptoms may be present) for 60 minute exposure 0.05 mg/l, for 8 hour 129
exposure 0.02 mg/l. At 1 part to 500 parts in air, HCN is instantaneously fatal. In the pure state death 1221
may be produced by the mere fraction of a gram.

(3) May be absorbed by inhalation or via the unbroken skin (liquid HCN as such; the cyanide ion is not 1221
absorbable via the unbroken skin). The cyanide ion may be absorbed from all other tissues than the 539
intact skin.

(4) In considering the toxicity of HCN per se, due regard must be paid to the toxicity of the substances, e.g. 1221
KCN, NaCN, $Ca(CN)_2$ from which it may be generated for use as a gas. The cyanide ion, CN^-, is the 2900
agent of toxic action in the body and an intake of 37.8 mg or more (as CN^-) may be fatal to man. Intake 3194
of 2.9-4.7 mg (CN^-) per day has been reported not harmful.

(5) At pH 8 or less, HCN in water is largely undissociated. Thus, toxicities expressed in terms of CN^- mean that most of the cyanide is in the form of HCN. When soluble cyanides, such as KCN and NaCN, are dissolved in water dissociation takes place, but CN^- reacts with $H^+ \rightarrow HCN$. The ratio of CN^- to HCN is a function of pH. At pH 7 or lower less than 1% of the cyanide is in the form of CN^-; at pH 8 only 6.7%; at pH 9 42%; at pH 10 87% of the cyanide is in the form of CN^-.

(6) Susceptibility of fishes to CN^- is affected by temperature and the concentration of dissolved O_2; high temperatures and low O_2 values enhance susceptibility.

(7) HCN is not bactericidal or fungicidal.

b) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Frog	sc	LD	60		1037
Mouse	sc	LD	5		1621
Mouse	sc	LD	3-10		1037
Mouse	ip	LD	3-10		1037
Guinea Pig	sc	LD	0.1		1037
Rabbit	or	LD	4		1037
Rabbit	sc	LD	1.1-3.0		1037
Rabbit	iv	LD	0.1-0.3		1037
Sheep	or	LD	1.05		2400
Cat	sc	LD	1.1		1037
Cat	inh	LC	0.2 mg/l; 181 ppm	Death with 5-10 min. exp.	1037
Cat	inh	LC	0.35 mg/l;317 ppm	Immediate death.	1037
Birds	sc	LD	0.1		1037
Dog	inh	LC	0.2 mg/l;181 ppm	Death with 5-10 min. exp.	1037
Dog	inh	LC	0.35 mg/l;317 ppm	Immediate death.	1037
Monkey	inh	LC	0.2 mg/l;181 ppm	Death with 5-10 min. exp.	1037
Monkey	inh	LC	0.35 mg/l;317 ppm	Immediate death.	1037
Trout	Medium	LC	0.10-0.15 ppm		678
Lagodon rhomboides (fish)	Medium	TL$_m$*	0.069 ppm	*=Median Tolerated Limit.	690
Trout (Black Hills)	Medium	LD$_{100}$	0.05 ppm	Exposure 120 hrs.	1749
Trout (")	Medium	LD$_{100}$	1.0 ppm	Exposure 20 min.	1749
Trout (Rainbow)	Medium	MLC	0.1-0.2 ppm	Exposure 1-2 days.	2927
Trout	Medium	CTO*	0.126 ppm	Concentration for turnover; exp. 170 min.	2400
Trout	Medium	CTO	0.15 ppm	Exposure ca. 5-64 min.	2928
Trout	Medium	CTO	0.42 ppm	Exposure 11 min.	2400
Trout	Medium	Survived	0.02 ppm	Expsoure 27 days.	1749
Trout	Medium	non-Toxic	0.084 ppm		2400
Bluegill	Medium	Survived	0.25 ppm		2400
Bluegill	Medium	Survived	0.4 ppm	Exposure 96 hrs.	2400
Bullhead	Medium	Survived	0.375 ppm		2400
Bullhead	Medium	Survived	0.5 ppm	Exposure 96 hrs.	2400
Fish	Medium	MLC	0.05-0.1 ppm		598
Fish	Medium	MLC	0.1 ppm		2056,2398
Fish	Medium	LC$_{100}$	0.2 ppm	Rapid mortality.	1959

c) Toxic and lethal dosages reported from stock-watering experiences:
Dog: 30-40 mg; Cow: 390-920 mg; Horse: 390 mg; Sheep: 40-100 mg. Water containing 103 ppm 2400
CN^- is fatal to ducks and cows.

d) Experiences in the feeding (to rats) of HCN fumigated food: 1611

(1) No overt signs of toxicity with foods containing 100-300 ppm of HCN.

(2) No gross or microscopic pathology on the foregoing diet.

(3) With food containing 100 ppm no free CN^- present in plasma, liver, kidneys but in most instances it was present in erythrocytes.

(4) Plasma, liver, kidneys and red cells revealed thiocyanate levels higher than in controls.

(5) Among animals on foods containing 300 ppm HCN no free CN^- was found in plasma, or kidneys; occasionally it was present in the liver and in the erythrocytes of less than 50% of the experimental group.

e) Pharmacological, pharmacodynamical, physiological, etc., higher animals:

(1) Mode of action: Reversible inhibition of iron—(ferric) containing cell respiratory enzymes. Cytochrome oxidase is most sensitive; inhibition blocks all oxidations dependent on cytochrome oxidase. 2994

(2) Cytochrome oxidase—CN$^-$ complex is dissociable; conversion of CN$^-$ to SCN$^-$ restores, in time, the enzymic activity.

(3) CN$^-$ does not react with haemoglobin. Reacts with Fe^{+++} of methaemoglobin, but affinity for the latter is less than for cytochrome oxidase. Competition is great in presence of large concentrations of methaemoglobin, thus holding cytochrome oxidase blockage to a minimum. 20

(4) CNS effects: Via the carotid and aortic bodies' chemoreceptors, respiration is stimulated by CN$^-$ in low concentration. The oxidative metabolic block elicits the response associated with relative anoxia in the chemo-receptor cells.

(5) Brain depressed; first the cortex then (in order) basal ganglia, hypothalamus, mid brain. Pons and brainstem may reveal moderate to no depression of electrical activity. Cord grey matter electrical activity is enhanced. Recovery is in the inverse direction. The effect of low CN$^-$ dosages is one of passing decerebration. Repeated daily dosages (insufficient for unconsciousness or convulsion) induce no central nervous pathological changes. 3226

(6) Cardiovascular effects: Signs of anoxia.

(7) Symptoms of poisoning with CN$^-$: Appear within seconds to minutes of ingestion or inhalation. Giddiness, hyperpnaea, headache, palpitation, cyanosis, unconsciousness; before death asphyxial convulsions may occur. Exceptionally, death may be delayed for as much as 3 hrs. 1221

(8) Treatment: Specific, but must be prompt. The aim is to induce, by sodium nitrite (0.3-0.5 g in 10 cc water by slow injection), methaemoglobinemia. CN$^-$ + methaemoglobin → cyanomethaemoglobin which, by later sodium thiosulfate (slow injection of 12.5g in 50 cc water) treatment, is then followed by metabolic conversion of CN$^-$ to SCN$^-$ which is eliminated. Adrenalin and O$_2$ may be needed to control hazardous side effects of sodium nitrite and methaemoglobin—CN$^-$ induced anoxemia. The preceding treatment is 4-5 times as effective as the methylene blue treatment formerly applied. Amyl nitrite inhalations may be supportive if brief delay must precede specific treatment.

f) Phytotoxicity:

(1) Phytotoxic for green plants, but not usually hazardous at insecticidal vapor concentrations. Night fumigation under dry conditions (either in tent or glasshouse) minimizes the phytotoxic hazard. Plants in daylight absorb HCN more readily than in darkness. Wet leaf surfaces and high humidity (permitting HCN solution on the plant) induce further damage. 539,1916

(2) At 0.13 mg/l, 3 hour exposure, some damage to carnations. 281

(3) At 1000 ppm damage to tomato, buckwheat, tobacco plants in ca. 15 minute exposures; leaf injury to tobacco in 4 minutes, to buckwheat and tomato in 12 minutes; stem injury to buckwheat in 60 minute exposures. 3086

(4) Serious damage to green vegetables, potato tubers, banana fruits. 539

(5) Moderate fumigation temperatures (70°-80°F down to 45° F) minimize phytotoxic hazard (below 45°F the kill of insect pests is less satisfactory). 1916

(6) Hazardous to fumigate, within 6 months, citrus trees treated with Bordeaux mixture; severe leaf burn and defoliation may occur. 1916

(7) Fumigation of citrus ordinarily done when fruit is size of a walnut. Lemons more resistant than others. Trees are most sensitive to HCN in late spring to early summer, in period of active growth and metabolism. Late winter and spring are best for citrus scale fumigation. 1916

g) Toxicity for insects:

Quantitative:

(1) Toxicity of HCN for 8 species of stored products insects exposed at 70° F in 100 ft^3 empty fumatoria for 2 and 6 hr. periods: 2005

Insect		LC$_{50}$(mg/l)		LC$_{95}$(mg/l)	
		2 hrs.	6 hrs.	2 hrs.	6 hrs.
Acanthoscelides obtectus	(adult)	1.5	0.9	4.5	2.7
Oryzaephilus surinamensis	(")	0.6	<0.4	1.4	1.2
Rhizopertha dominica	(")	1.2	0.8	4.4	2.6
Sitophilus granarius	(")	23.0	4.6	90.0	9.9
Sitophilus oryzae	(")	20.0	2.8	26.0	5.9
Stegobium paniceum	(")	0.5	<0.4	1.0	0.7
Tribolium confusum	(")	1.0	0.8	2.2	1.6
Zabrotes pectoralis	(")	1.4	1.0	4.4	2.7

(2) Toxicity of HCN at various stages in the life-cycle of Tribolium confusum; order of resistance: Pupa (most resistant) > adult > larva > egg: 1231

Stage		mg/l HCN For 50% Kill
Egg (1 day old)		0.195 ± .007
Egg (3-4 days old)		.326 ± .007
Larva (20 days old)		.439 ± .015
Pupa (0-1 day old)	♂	.659 ± .015
	♀	.639 ± .018
Pupa (2-3 days ")	♂	1.216 ± .023
	♀	1.363 ± .035

(2) Toxicity of HCN at various stages in the life-cycle of Tribolium confusum; order of resistance: Pupa (most resistant) > adult > larva > egg: 1231

Stage		mg/1 HCN For 50% Kill
Pupa (7-8 days old)	♂	.817 ± .022
	♀	.729 ± .020
Adult (0-1 day old)	♂	.810 ± .085
	♀	.919 ± .060
Adult (14 days old)	♂	.750 ± .031
	♀	.569 ± .038
Adult (28 ")	♂	.703 ± .025
	♀	.479 ± .040

(3) Toxicity of HCN as reported by various workers for various insects:

Insect	Route	Dose	Dosage (mg/l)	Remarks	
Cimex lectularius (egg)	Fumig	LC_{95-100}	< 0.4	5 hrs exp., 25°C, in 12 l flasks (empty).	2622
Cimex lectularius (egg)	Fumig	LC_{50} 5 days	0.096	" 6.4 l " .	1292
Cimex lectularius (older nymphs)	Fumig	LC_{95-100}	0.4	" 12 l " .	2622
Cimex lectularius (nymphs, 2,3 instar)	Fumig	LC_{50} 48 hrs	0.331	" 6.4 l " .	1292
Cimex lectularius (adult)	Fumig	LC_{95-100}	< 0.4	" 12 l " .	2622
Cimex lectularius (adult	Fumig	LC_{50} 48 hrs	0.336	" 6.4 l " .	1292
Cimex lectularius	Fumig	LC	0.17	5 hrs exp., 25°C. " .	412
Dacus dorsalis (23-26 hr naked egg)	Fumig	LC_{50}	10.0	2 hrs exp., 71°-80°F, empty vessel.	255
Dacus dorsalis (")	Fumig	LC_{95}	26.0	" " "	255
Dacus dorsalis (3rd instar)	Fumig	LC_{50}	1.3	" " "	255
Dacus dorsalis (")	Fumig	LC_{95}	2.8	" " "	255
Drosophila melanogaster (adult)	Fumig	LC_{50}	1.26	Ca. 7 minute exposure.	353
Ephestia kühniella (larva)	Fumig	LC_{50}	0.4		417
Sitophilus granarius (adult)	Fumig	LC	14.0	5 hrs exp., 25°C.	412
Sitophilus granarius (adult)	Fumig	LC_{50}	22.0		417
Sitophilus granarius (")	Fumig	LC_{50}	5.8	5 hrs exp., 25°C, empty flask.	156,2816
Sitophilus granarius (")	Fumig	LC_{99}	11.4	" " "	156,2816
Sitophilus granarius (")	Fumig	LC_{100}	ca. 13.0	" " "	2487
Sitophilus oryzae (adult)	Fumig	LC	12.0	5 hrs exp., 25°C.	412
Sitophilus oryzae (")	Fumig	LC_{50}	24.0		417
Tineola biselliella	Fumig	LC_{50}	6.5		417
Tribolium castaneum (adult)	Fumig	LC	0.36	5 hrs exp., 25°C.	412
Tribolium castaneum (")	Fumig	LC_{50}	0.6		417
Tribolium confusum (adult)	Fumig	LC_{50}	0.6	5 hrs exp., 25°C, empty flask.	156,2816
Tribolium confusum (")	Fumig	LC_{50}	0.607		2995
Tribolium confusum (")	Fumig	LC_{50}	0.57		2816
Tribolium confusum (")	Fumig	LC_{50}	0.63		2816
Tribolium confusum (")	Fumig	LC_{99}	1.1	5 hrs exp., 25°C, empty flask.	156,2816

(4) Toxicity of HCN for Tribolium confusum and Sitophilus granarius (adults) exposed in whole grain wheat at various depths in 28 liter cans 14.5 in. high, 12.5 in. diameter holding 30 lbs wheat 8 in. deep, with 6.5 inches free space above the grain surface. mg/1 ÷ 16 = lbs/1000 ft^3. Exposure 24 hrs, at 80°F: 2009

Position Of Insects In Wheat (Depth; Inches)	Tribolium confusum		Sitophilus granarius	
	LC_{50}(mg/l)	LC_{95} (mg/l)	LC_{50}(mg/l)	LC_{95} (mg/l)
At Surface	< 2.5	< 2.5	< 2.5	31.0
2	5.9	12.3	7.6	36.4
5.5	16.0	39.0	9.6	60.4

(5) Mortality of Ephestia elutella and Lasioderma serricorne with open warehouse HCN fumigation, at 24 hrs. exposures: 2591

Ounces/1000 ft^3	°F	% Mortality Lasioderma			% Mortality Ephestia		
		Adults	Larvae	Eggs	Adults	Larvae	Eggs
8	82	100	100	100	100	100	100
6	70	93.8	100	100	100	100	100
6	71	83.7	77.3	100	100	100	100
Control	74	0	3.2	2.6	30.7	4.6	52.9

Does not readily penetrate cigars; for Lasioderma serricorne, in cigars, 2 lbs per 1000 ft^3, with exposure of 15-24 hrs. was required for 100% kill; 3 lb per 1000 ft^3, with 4 hrs. exposure and a vacuum of 26 inches, gave 100% kills. 661

(6) Toxicity of HCN (alone, and with auxiliary gases) for 4 species of insects: 2537

HCN % By Wgt In Air	Exposure (Minutes)	% Mortality Of			
		Hippodamia convergens	H. ambigua	Cryptolaemus montrouzieri	Sitophilus granarius
0.2	10	85	70	15	0
0.2	20	95	95	95	0
0.2	30	100	100	100	0
1.0	30	–	–	–	20
2.0	30	–	–	–	30
3.0	30	–	–	–	90
4.0	30	–	–	–	100

Auxiliary gases were effective in shortening the exposure time for kill of Hippodamia convergens to 15 minutes or less. HCN 0.2% by wgt. plus:

Gas (auxiliary)

Salicyl aldehyde gave 100% kills in 10 min at 0.025, 0.05 %
" " gave 100% kills in 5 min at 0.1%
Benzaldehyde gave 100% kills in 15 min at 0.05%; at 10 min at 0.1%
Ethyl thiocyanate, Allyl thiocyanate } gave 100% kills in 15 min at 0.01%; 10 min at 0.05%
Thiophenol gave 100% kills in 20 min at 0.05%; 10 min at 0.1%
Benzyl bromide, Perchlormethyl mercaptan } gave 100% kills in 10 min at 0.1%

(7) Effects of various air pressures on the mortality of insects exposed to HCN in 10 minute exposures: 2297

Air Pressure (mmHg)	Kill Of Sitophilus oryzae At 20°C With HCN		
	3.19 mg/l	4.65 mg/l	7.15 mg/l
2	0	0	0
10	–	30.9	37.2
14	–	52.3	–
20	66.2	69.6	83.2
30	–	74.7	–
40	80.3	78.1	98.9
50	–	82.2	–
60	79.4	84.8	96.4
70	–	87.5	–
80	83.3	83.9	94.4
100	62.5	72.5	90.7
150	–	–	69.6
200	–	–	43.6
400	–	–	17.4
760	–	–	0

(8) Effect of air pressure on various insects fumigated with HCN in 10 minute exposures, at 25°C: 2297

Insect	HCN (mg/l)		% Mortality At			
			2 mmHg	30 mmHg	60 mmHg	90 mmHg
Lasioderma serricorne	1.06		51.9	73.8	74.4	66.8
" "	1.52		81.1	98.1	93.0	85.6
" "	0.36		69.9	79.1	58.8	56.9
Sitophilus granarius	7.19	(1 hr exp.)	6.1	89.3	78.4	–
Flat grain beetle	1.45	(" ")	10.3	46.3	50.7	–
Saw toothed grain beetle	0.46	(" ")	30.0	–	79.6	–
Lesser grain borer	1.45	(" ")	78.0	77.1	74.5	–

(9) Effect of varying degrees of vacuum on the effectiveness of HCN fumigation of flour vs. Tribolium confusum, exposed for 1 hr in the middle of 48 lb bags of flour in a 14 ft^3 fumatorium: 3389

Initial Vacuum Drawn	Dose HCN (liquid) (oz.)	Temp. Flour (°F)	% Mortality
26	3/8 (ca 10.65 g)	65	4
26	4/8 (" 14.2 g)	65	65
26	5/8 (" 17.75 g)	65	15
26	6/8 (" 21.3 g)	63	100
28	1/8 (" 3.5 g)	60	17
28	2/8 (" 7 g)	60	100
29	1/8 (" 3.5 g)	60	100

(10) HCN in the fumigation of nursery stock vs. Aspidiotus perniciosus: 222

① Concentration (g/m^3)	② Fumigation Time (Hrs.)	①X②	% Kill
5	.05	.25	98.1
5	.1	.5	100
5	.15	.75	100
14	.118	.25	92.4
14	.035	.5	99.8
14	.071	1	100
2.5	.1	.25	96.4
2.5	.2	.5	99.6
2.5	.4	1.0	99.8
2.5	.8	2.0	100
2.5		3.0	51.9

h) Resistance of certain insects toward HCN; selective effect of HCN exposure in the appearance of resistant biotypes:

(1) The first clear cut demonstration of the selection of resistant biotypes of insect species by exposure to insecticides was made with HCN and Aonidiella aurantii. A few examples follow: 2559

(2) Repeated HCN fumigation and resistance of Aonidiella aurantii; 2006
Resistant and non-R races sampled at 2 yr. intervals (scale generations per year = 9):

HCN (mg/l)	% Mean Mortality In Year							
	1938		1940		1942		1944	
	R	Non-R	R	Non-R	R	Non-R	R	Non-R
0.19	50.2	95.0	47.0	95.6	43.6	97.3	46.5	96.6
0.36	67.4	97.5	63.3	98.7	62.6	99.4	60.3	98.9
0.54	81.0	96.3	80.9	99.7	81.3	100	74.9	99.4
0.70	84.0	100	91.3	99.9	87.3	99.8	81.8	100
0.90	89.4	—	93.9	100	91.5	99.9	90.0	99.7
1.0	96.2	100	92.0	100	93.5	99.9	94.0	99.4

Repeated fumigation over a period of years of a strain originally non-R:

HCN (mg/l)	Mean % Mortality					
	Culture 1			Culture 2		
	Original Strain	After 4 Fumig	After 9 Fumig	Original	After 6 Fumig	After 4 Fumig
0.19	99.0	97.2	28.7	98.7	91.1	81.7
0.36	99.3	99.3	99.5	100	99.4	96.0
0.54	99.8	99.6	99.9	100	99.9	99.8
0.70	100	99.5	100	—	99.9	100
0.90	—	—	99.8	—	100	100
1.0	—	—	100	—	100	100

Effects of repeated fumigation on a culture originally non-R, but with some resistant individuals probably present:

HCN (mg/l)	Mean % Mortality	
	Original	After 5 Fumigations
0.19	94.5	37.7
0.36	97.9	65.7
0.54	99.6	76.4
0.70	99.8	79.8
0.90	99.6	91.7
1.0	—	93.8

Effect of repeated fumigations on cultures originally resistant:

HCN (mg/l)	Mean % Mortality							
	Culture 7				Culture 8			
	Original	After 6	After 11	After 16	Original	After 7	After 12	After 18 (Fumigations)
0.19	50.2	26.0	14.0	12.7	56.0	26.3	14.6	10.7
0.36	67.4	55.5	30.3	28.1	65.1	38.3	36.9	25.5
0.54	81.0	78.5	47.0	49.0	80.7	58.6	40.4	48.0
0.7	84.0	82.9	58.7	62.2	89.6	80.8	71.2	76.0
0.9	89.4	89.7	79.7	81.7	91.0	97.0	81.6	79.0
1.0	96.2	91.0	87.1	91.2	—		87.4	88.7

(3) HCN fumigation of Aonidiella aurantii, R and non-R strains; tent fumigation with steady leakage and decline in concentration during exposure period and low uniform concentrations in air-tight fumatorium tests: 2002

Tent Fumigation (Exposure 45 min.)				Fumatorium (Exposure 45 min.)			
Dosage (cc at peak)	mg/l	Mean Kill (%)		Dosage (cc)	(mg/l)	Mean Kill (%)	
		non-R	R			non-R	R
4	0.299	98.44	59.37	1	0.198	94.93	50.21
8	.479	99.29	76.48	2	.427	98.69	67.44
10	.534	99.63	85.29	3	.528	99.43	80.84
12	.603	99.79	87.36	4	.713	99.54	84.06
14	.728	99.84	89.53	5	.817	99.85	89.38
16	.820	99.95	94.61	6	—	—	96.21
18	.913	100	94.17	8	—	—	99.32
20	.981	99.98	95.69	—	—	—	—
22	1.209	99.94	97.16	—	—	—	—
24	1.215	100	96.92	—	—	—	—
26			97.08	—	—	—	—

High mortality of non-R strain with low dosage and short exposures (differences between 15, 30, 45 minute exposures being slight.

Unsatisfactory results with low dosage and short exposures in the R strain.

(4) Resistance to HCN in Tribolium confusum: 1231

Offspring of survivors of HCN fumigation found to have an LC_{50} 60% higher than the ordinary laboratory strain. The resistant strain showed a greater O_2 uptake (2.8 vs. 2.2 mm^3/mg).

(5) Resistant biotypes have been demonstrated for Aonidiella aurantii, Saissetia oleae, Citricola scale and Coccus pseudomagnoliarum. 2559 2560

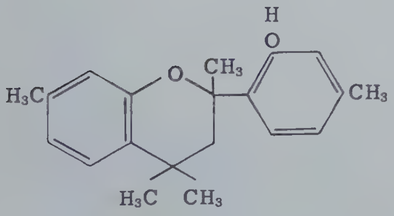
i) Comparative toxicity, HCN and other fumigants:

(1) Tabular data of a comparative nature may be found by consulting, in this work, the general treatment titled Fumigants.

102

HYDROXYPENTAMETHYL FLAVAN

(2 -Hydroxy-2, 4, 4, 7, 4′-pentamethyl flavan; Dimeric form of 4-Isopropenyl-m-cresol.)



Molecular weight 296.312

GENERAL

Not, properly speaking, an insecticide in the ordinary sense of the term. The substance was introduced as an acaricide or rather as a compound having a mechanical entangling or trapping effect on mites, etc. An inert, gummy film is left on foliage after spraying which hinders or obstructs the movement of acarines and small insects. No longer available commercially. Included here because recent data (vide infra) indicate a usefulness in the control of chiggers on woodland plots. 3160

PHYSICAL, CHEMICAL

An opaque, sticky material or an amorphous glass which, from ether solution, crystallizes in colorless plates; m.p. (crystalline) 76°-77°C; v.p. very high; under reduced pressure distills without change; the crystalline form has one ether of crystallization and the following empirical formula: $C_{20}H_{24}O_2 \cdot (CH_3)_2O$ and loses the ether of crystallization on exposure; the hydroxyl group has weak phenolic properties; a crystalline, monoacetyl derivative may be prepared.

TOXICOLOGICAL

1) No toxicological data are available to this compilation. Considered to be relatively inert biologically.

USES

1) Added as a 0.1% suspension to late-season DDT orchard sprays, hydroxypentamethyl flavan is reported to hold acarine infestation at low levels although some fruit discoloration and foliage injury may be present. 2448 677

2) Excellent results have been reported in control of Acariscus mansoni and Eutrombicula alfreddugesi (Chiggers) with applications at 2 lb per acre, as the following tabulation giving comparative data for several insecticidal and acaricidal substances indicates: 2863

Compound and Rate/Acre active as spray			Count Of Chiggers* Before Treatment	% of Original Infestation (Count At Days After Treatment)							
				1 day	3-5 days	7-9 days	10-14 days	15-19 days	21-24 days	29-36 days	42-58 days
HPMF**	5	lb	105	0	3	11	—	11	—	7	9
"	8	lb (dust)	98	4	1	—	—	0	—	0	0
"	4	lb (")	269	1	2	2	—	3	—	0.4	1
"	4	lb	150	2	1	2	—	1	2	1	—
"	1	lb	136	2	3	1	6	15	—	—	—
"	.75	lb	104	6	—	—	9	0	4	—	—
"	2	lb	115	3	—	1	2	—	0	—	—
DDT	10	lb	66	59	47	—	—	100	99	101	100
BHC	5	lb	105	0	0	3	—	11	5	7	—
"	1	lb	150	3	43	50	10	71	—	—	—
"	0.75	lb	127	3	—	—	3	12	3	—	—
"	2	lb	252	0	—	0.4	2	—	2	—	—
Derris***	16	lb	84	90	—	26	8	—	48	—	—
Dimethyl phthalate	5	pints	169	61	80	89	74	—	159	—	—
Dibutyl phthalate	5	pints	122	8	18	18	36	—	54	—	—
Benzyl benzoate	5	pints	109	7	21	37	41	—	81	—	—
Sulfur (wettable)	104	lbs	74	14	0	—	—	11	36	24	8
" "	100	lbs	67	6	0	0	—	4	1	1	—
" "	48	lb	177	5	—	12	—	2	21	—	—
Sulfur	100	lb	64	2	2	3	—	6	2	3	—
"	48	lb	117	14	—	15	—	1	25	—	—
Control			160	54	45	71	65	—	86	77	108
"			44	91	214	—	—	143	155	259	70
"			64	113	113	148	—	144	177	86	—
"			98	95	78	26	78	52	—	—	—
"			84	106	—	—	44	38	32	—	—
"			76	44	—	101	44	38			
"			72	132	—	104	—	100	38	—	—

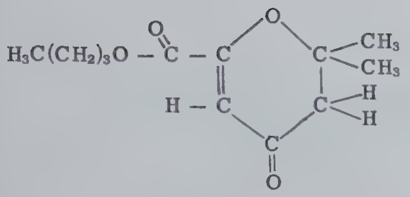
*Number collected in a 1 minute exposure of 1 ft^2 of cloth.

**Hydroxypentamethyl flavan.

***4% rotenone content.

103

INDALONE® (2, 2-Dimethyl-6-carbobutoxy-2, 3-dihydro-4-pyrone; Dihydropyrone; α,α-Dimethyl-α′-carbobutoxy-dihydro-γ-pyrone; 2-Carbo-n-butoxy-6, 6-dimethyl-5, 6-dihydro-1, 4-pyrone; n-Butyl ester of 3, 4-Dihydro-2, 2-dimethyl-hexo-2H-pyrone-6-carboxylic acid; n-Butyl mesityl oxide oxalate; Butopyronoxyl (USP).)



Molecular weight 226.26

GENERAL [Refs.: 3158,353,774,1804,3116,2948,1828,314,1059,1131]

A substance repellent to certain insects, but possessing little if any insecticidal activity. Harmless as a skin application for warm-blooded animals. An effective clothing impregnant, withstanding several days wear (at least 10 days) while still retaining repellency when used at rate of 2g per ft^2 of cloth (approximately 5% of dry weight). Ordinarily used as a component of a repellent mixture, for instance the mixture designated as "6-2-2" which was for long dispensed as a standard all-purpose repellent for use of troops and which contains 6 parts dimethyl phthalate, 2 parts Indalone® and 2 parts 2-ethyl-1,3-hexanediol.

PHYSICAL, CHEMICAL

A yellow to red-brown liquid with an aromatic, somewhat "burnt" odor; thin and oily in consistency; b.p. 256-270°F, 113°C; $d^{25°}_{25°}$ 1.05-1.06; $n^{25°}_{D}$ 1.47; virtually insoluble in water; miscible with alcohol, chloroform, ether and glacial acetic acid.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Generally considered non-poisonous to mammals. Harmless as a skin application for warmblooded forms. Dibutyl oxalate, present as an unreacted impurity (Indalone® is made from dibutyl oxalate and mesityl oxide by condensation in the presence of sodium ethoxide) is undesirable, being absorbable by the skin and injurious to the kidneys.

Animal	Route	Dose	Dosage (cc/k)	
Mouse	or	LD_{50}	11.6	842
Rat	or	LD_{50}	7.4	842
Guinea Pig	or	LD_{50}	3.2	842
Rabbit	or	LD_{50}	5.4	842
Chicken	or	LD_{50}	15.0	842

2) Toxicity for insects and acarines:
   a) There is no evidence to indicate that Indalone® is particularly toxic to insects.
      (1) A low order of toxicity for the larvae of Carpocapsa pomonella is reported. 2831
      (2) Spoken of by some as toxic to flies and mosquitoes, although screening tests find Indalone® at best, 1059
      ranged among compounds of generally mediocre action; this is true for lice, (adults, eggs), mosquitoes 1801
      (larvae), fleas, ticks, Periplaneta americana and Blattella germanica. 1131
      (3) "Knockdown" capacity of Indalone® for chiggers is apparently rather high. 1801
   b) The pyranone derivative of Indalone® is reported as toxic to Musca and mosquitoes, as well as being 1131
   bactericidal and fungicidal. The toxicity is associated with the -C = C – C = O- grouping and is manifested also by piperine (which is highly insecticidal), anisolactone (toxic for maggots) acrolein, crotonaldehyde, mesityl oxide, allyl formate, ethyl acrylate and such pediculicides as diallyl succinate and diallyl fumarate. Such substances are stated to combine with sulfhydryl (SH^-) groups.
   c) Repellency:
      (1) A succinct treatment of the general subject may be found in Ref. 774.
      (2) In repellency tests (with rabbits as "bait") 5% solutions of Indalone®, impregnated on cheese cloth, 2950
      gave the following results vs. Stomoxys calcitrans:

% Repellency On Stated Days After Treatment				
1 day	4 days	7 days	10 days	14 days
99.3	92.1	88.8	82.3	71.0

(3) Screening tests showed good to very superior repellency on skin and/or clothing for *Aëdes aegypti*, *Aëdes sollicitans*, *Aëdes taeniorhynchus* and *Anopheles quadrimaculatus* with good wearing qualities for some, and relatively poor for others. Does not withstand washing with a persistence of repellency. In "patch" and "pen" tests, superior repellency for *Amblyomma americanum* is reported. 1801

104

INSECTICIDAL FUMIGANTS (GENERAL CONSIDERATIONS, COMPARATIVE TABLES, DATA)

1) DEFINITION

Insecticidal fumigants are those substances used to kill insects and related forms by application as gases or vapors. 353,1059 156,2815,757

2) TOXICOLOGICAL

a) Determinations of insect toxicity of fumigants are complicated by numerous variables, among them:
   (1) Difficulty of distinguishing a sharp end-point for mortality.
   (2) Speed of action of a particular substance; some substances act rapidly, paralyze quickly, others are slow acting and anaesthetic in effect.
   (3) Characteristics of individual insect species and types, stage of development and environmental circumstances complicate the choice of end-points. For example, *Plodia interpunctella* larvae, fumigated with carbon disulfide, have revived a week or more after treatment to complete their development to the adult reproductive stage. 1365

b) The *most precise estimate* of relative dosages from mortality curves is made at the point of 50% mortality, the *Median Lethal Concentration*, or LC_{50}.
   (1) LC_{50} has certain disadvantages as ground for establishing relative practical value of fumigants:
      (a) Mortality curves are rarely parallel and may even cross between the 50% and 100% mortality points, an example being the curves for chloropicrin and ethylene oxide whose LC_{50} values would indicate equivalent toxicities, whereas the LC_{100} establishes ethylene oxide as considerably more effective than chloropicrin.
      (b) Although less precise, estimates at a point near 100% mortality are more suitable than LC_{50} estimates in considering the *practical* application of fumigants.
      (c) Statistical considerations make comparisons of dosages that produce 100% kill inadvisable if each dosage is estimated from the upper end of a toxicity curve. The following equation has been suggested by which an estimate is calculated from two points on a more reliable part of an experimental curve, namely at points of 50% and 90% mortality: 156

$$X = K + k \cdot \log \frac{y}{100-y} \quad \text{where:}$$

K = dosage to yield 50% mortality,
k = " " 90% " ,
X = value for dosage,
y = value for mortality.

c) *Toxicity and temperature*: Temperature variously affects fumigants:
   (1) Volatility increases with increase of temperature.
   (2) Surface absorption decreases with increase of temperature.
   (3) Physiological state of the exposed insect alters with increasing or decreasing temperature.
   (4) Insect susceptibility changes with increasing or decreasing temperature.
      (a) The mortality of an insect species may be greater at a lower temperature, which favors adsorption of a gas, than at a higher temperature, which favors or enhances its chemo-physiological action. Thus, since adsorption of fumigants on treated materials is greater at lower temperatures, the enhanced adsorption may more than offset the chemo-physiological factor for insects exposed at low temperatures.

d) *Penetration of fumigants*:
   (1) Efficiency of fumigation with a liquid depends (among other variables) on the vapor pressure, or vaporization tendency, for instance at 25°C (77°F) water and chloropicrin have an equal vapor pressure while ethylene chloride has 3.4 times, carbon tetrachloride 4.9 times, carbon disulfide 15.2 times the vapor pressure of water.
   (2) Fumigants which are normally gases at the fumigation temperature are not limited as above. Their introduction into a space to be treated depends on method or equipment.

(3) The concentration of a fumigant which, in a given space and at a given temperature, can exist as a vapor is an important consideration and has for many fumigants been calculated. 2670

(4) Once a fumigant is in the vapor state, the problem of penetration becomes a problem of diffusion.

- (a) Mass movement (by air currents) as distinct from true molecular diffusion to a large extent equalizes the concentration of a gas in a space, for example hydrocyanic acid gas rising from a chemical generator or carbon disulfide vapor falling from a suspended vessel.
- (b) Distribution of a liquid fumigant by sprinkling or other forms of dispersion; enhancing its distribution by means of fans or blowers aids in quick achievement of a uniform mixture with air.
- (c) Molecular diffusion procedes more slowly. Fumigants of lowest molecular weight diffuse more rapidly, for instance, hydrogen cyanide, carbon dioxide and ethylene oxide, other things being equal, diffuse more rapidly than chloropicrin, carbon tetrachloride or ethylene dichloride. Diffusion is important in the penetration by a gas of furniture or packaged materials and is an important factor in the loss of a fumigant from a treated space.
- (d) Two factors interact: Diffusion (rate depending on molecular weight and size of opening through which the fumigant passes) ⇄ absorptive capacity of the material through which diffusion is occurring. Thus the absorptive capacity of a material must be satisfied before a stable concentration can be maintained in the surrounding atmosphere. For example, in an empty vacuum tank it was found that two ounces of chloropicrin for 100 ft^3 was needed to give 100% kills of Tribolium confusum at 72°F in two hour exposures. The same tank being filled with raw peanuts, 48 ounces of chloropicrin was necessary to give 100% mortality under similar exposure and temperature. Of ethylene chloride 3.2 ounces per 100 ft^3 were needed for 100% kill in the empty tank and 11.2 ounces in the peanut filled space. 607

(5) Relative ease or difficulty of penetration of a fumigant is a prime factor. 2996

- (a) Heavier fumigants, for example carbon disulfide and chloropicrin, do not sink far into a mass of grain unless aided by mixing, stirring, etc., and concentration varies inversely with depth below the surface.
- (b) Adsorption of gases by top layers impedes rapid downward movement into the grain mass.
- (c) Ventilation of a treated space results in a lessening concentration of fumigant, first in the open spaces. Diffusion gradient is reversed, being from, rather than into the fumigated material. The gas may diffuse out as slowly or rapidly as it went in, the outward diffusion rate depending on the same factors as the inward rate. Thus since a low concentration of a toxic gas may be lethal if the exposure is sufficiently long, enough fumigant may be retained to be effective in killing insects in a treated material even if penetration is relatively slow. 2755

3) TABULAR ILLUSTRATIONS OF CERTAIN OF THE GENERAL PRINCIPLES OUTLINED ABOVE:

I) Toxicity hazards of insecticidal fumigants and insecticide solvents. 1665

- a) Maximum Tolerated Concentrations (MTC) based on experiments with Guinea pigs. MTC indicates here the amount of a substance tolerable without serious symptoms (although slight symptoms may occur.)

Substance	MTC (mg/l)		Probable Safe Concentration For Indefinite Exposure	
	1 Hr Exposure	8 Hrs Exposure	mg/l	ppm
Chloropicrin	0.007	—	—	—
Hydrocyanic acid gas	.05	.02	—	—
Sulfur dioxide	.13	.02	—	15
Dichloroethyl ether	.22	.15	.10	—
Hydrogen sulfide	.24	.10	—	—
Carbon disulfide	1.5	1.0	.01	3.2
Methyl bromide	3.9	.19	.05	100
Ethylene oxide	5.4	.45	.45	250
Ethylene dichloride	10.2	2.9	.43	100
Methyl formate	10.9	3.3	3.7	1500
Carbon tetrachloride	60	10	.69	100
Benzene, Toluene, Xylene	10	5	.34-.48	100
Turpentine	—	—	4.0	700
Gasoline	—	—	4.0	1000

II) Volatility and insecticidal activity of fumigants based on LC_{50} for Tribolium confusum exposed at 25°C for 5 hrs: 2815

- a) Toxicity of fumigants (in general) is inversely related to boiling point, for example LC_{50} for Agriotes larvae declines 10 times for every 70° increase in b.p.; for Musca a 10-fold increase in toxicity has been shown for every 78° increase in b.p. and for Tribolium a 10-fold toxicity increase for every 73° rise in b.p. 2293 3060 355
- b) Toxicity is directly related to vapor pressure of a fumigant and to volatility, for instance fumigant toxicity rises (average) 10-fold for every 75° rise in boiling point for Musca; vapor pressure decreases 10-fold for every 50° rise in b.p. 2293

b) Toxicity is directly related to vapor pressure of a fumigant and to volatility, for instance fumigant toxicity rises (average) 10-fold for every 75° rise in boiling point for Musca; vapor pressure decreases 10-fold for every 50° rise in b.p. 2293

Fumigant	B.P.(°C)	V.P. At 25°C mmHg	Vapor Saturation 25°C* mg/l	LC_{50} For Tribolium confusum mg/l At 25°C
Sulfur dioxide	10	> 760	2670	6
Methyl bromide	5	1824	2860	11
Ethylene oxide	11	> 760	1800	18
Hydrocyanic acid gas	26	739	1140	.6
Carbon disulfide	46	361	1470	61
Carbon tetrachloride	76	114	940	185
Ethylene dichloride	84	80	430	38
Trichloroethylene	87	73	512	108
Chloropicrin	112	24	212	5
Dichloroethyl ether	175	1.1	23	1.6
Hexachloropropene	203	0.3	6.6	1.1
Heptachloropropane	240	0.09	1.4	2.5

*Molar concentration of vapor to saturate air at S.T.P. is a direct function of V.P.

III) Maximum weights, lbs per 1000 ft³, of various fumigants which can exist in vapor form in a 1000 ft³ fumigating chamber at various temperatures. V.P. in mmHg: 2671

Temperature (°F)	SO_2*	CS_2**		Chloropicrin**		CCl_4**		HCN**		Ethylene oxide**		Ethylene dichloride**	
	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³
32	179	127	36	5.7	3.4	33	19	264	26	316	51	24	8.6
59	169	246	65	13.8	8	71	38	500	47	760	116	49	17
68	167	297	77	18.3	10	91	48	610	56	760	114	63	21
77	164	357	91	23.8	13	115	59	739	67	760	113	80	26
86	161	433	109	31	17	143	73	760	68	760	111	100	33
95	158	519	128	40	21	176	88	760	67	760	109	125	40
104	156	617	150	51	27	216	106	760	66	760	107	154	49
113	153	729	175	65	34	263	127	760	65	760	105	189	55
122	151	760	179	81	42	313	149	760	64	760	104	230	71

Temperature (°F)	Tetrachlorethane**		Trichlorethylene**		Methyl formate**		Ethyl formate**		Ethyl acetate**		Paradichlorbenzene**		Naphthalene**		Nicotine**	
	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³	V.P.	lb/1000ft³
32	1.4	.9	23	11	241	53	64	17	24	8	.08	.04	.02	.01	—	—
59	4	2	44	20	431	90	164	42	55	18	.4	.2	.06	.03	—	—
68	5	3	57	25	516	106	207	52	73	22	.64	.3	.08	.035	.08	.04
77	6	4	73	32	614	124	255	62	92	27	1.0	.5	.1	.04	.12	.07
86	8	5	94	41	725	144	312	75	119	35	1.5	.7	.14	.06	.16	.09
95	11	6	119	51	760	148	382	92	148	42	2.3	1.1	.21	.09	.23	.12
104	14	8	149	63	760	146	462	109	186	52	3.4	1.6	.32	.13	.30	.16
113	18	10	185	76	760	144	558	130	230	64	5.1	2.4	.51	.21	.41	.22
122	23	12	224	91	760	142	668	153	282	77	7.4	3.4	.81	.32	.55	.28

*Gaseous at 32°F.
**Solid or liquid at 32°F.

IV) Gas concentrations of various fumigants; ($\text{ppm} = \frac{24{,}450 \text{ x mg}}{\text{molecular wgt}}$ $\text{mg/l} = \frac{\text{ppm x mol wgt}}{24{,}450}$ 2815

1 lb/1000 ft³ = 16.0189 mg/l; 1 mm³/l = 1 ppm; 1% by volume = 10,000 ppm.)

Substance	Mol. Wgt.	1 mg/l = ppm	1 ppm = mg/l
HCN	27	906	.001104
Formaldehyde	30	815	.001227
Ethylene oxide	44	556	.001800
Acrylonitrile	53	461	.002168
Cyanogen chloride	61	401	.002495
Sulfur dioxide	64	382	.00262
Carbon disulfide	76	322	.00311
Methyl bromide	95	257	.00389
Ethylene dichloride	99	287	.00405
Naphthalene	128	191	.00524
Dichloroethyl ether	143	171	.00585
Trichloroacetonitrile	144	170.3	.00589
p-Dichlorobenzene	147	166.3	.00601
Carbon tetrachloride	154	158.8	.00630
Nicotine	162	150.9	.00663
Chloropicrin	164	149.1	.00671
Ethylene dibromide	188	130.1	.00769

V) Influence of humidity on the toxicity of several fumigants for the eggs and adults of Tribolium confusum; LC_{50} for exposures of 5 hrs. at 25°C: 2008

Fumigant	Eggs		Adults	
	Low Humidity (no > 10% R.H.) LC_{50} (mg/l)	High Humidity (50-70% R.H.) LC_{50} (mg/l)	Low Humidity (no > 10% R.H.) LC_{50} (mg/l)	High Humidity (50-70% R.H.) LC_{50} (mg/l)
Chloropicrin	45	16	4.4	4.4
Carbon disulfide	147	87	63	63
Ethylene oxide	2	2	18	18

VI) Effect of O_2 lack on susceptibility of insects to some fumigants: 608

Insect	Stage	Fumigant	Vacuum Held At (inches)	LC_{100} (mg/l)	Exposure Time
Sitophilus oryzae	Adult	Ethylene oxide	0	48	30 min
S. oryzae	"	"	29	24	"
S. oryzae	"	Methyl chloroacetate	0	17	"
S. oryzae	"	"	29	8.5	"
Ephestia kuehniella	Larva	Ethylene oxide	0	80	"
E. kuehniella	"	"	29	35	"
E. kuehniella	Egg	Carbon disulfide	0	502	1 hr
E. keuhniella	"	"	29	502	"
Tribolium confusum	Pupa	Ethylene oxide	0	141	30 min
T. confusum	"	"	29	22	"

VII) Influence on the toxicity of fumigants of the presence of CO_2 in various concentrations. Test insect: Tribolium castaneum (adult) 1732,608,617 1457,1730,1820 2214,2173,2537 3301,3313

a) LC_{50}, LC_{100} values in mg/l of the fumigants used for T. castaneum adults exposure 5 hrs at 25°C:

Fumigant	LC_{50} ← (mg/l)	→ LC_{100}		
Methyl formate	17.81	25.0	Exposure	5 hrs.
Ethylene oxide	13.44	17.5	"	" .
Methyl bromide	6.13	8.75	"	" .

b) Exposure time necessary for 50% and 100% mortality of T. castaneum with selected concentrations of fumigants plus various percentages of CO_2:

CO_2 In Gas Mixture %	Exposure Time (hrs : min) Necessary For 50% And 100% Kills With					
	Methyl formate (25mg/l)		Ethylene oxide (17.5mg/l)		Methyl bromide (8.75mg/l)	
	50% Kill	100% Kill	50% Kill	100% Kill	50% Kill	100% Kill
0	2 hrs : 30 min	5:00	2:30	5:00	3:40	5:00
1.0	2:05	3:30	2:30	5:00	3:10	4:30
5.0	:45	2:30	1:22	3:00	2:25	4:00
10.0	:25	2:00	:36	1:30	2:05	3:00
20.0	:19	1:30	:22	:45	1:40	3:00
40.0	:17	:45	:22	:45	1:50	3:00
60.0	:17	:45	:17	:45	2:20	3:30
80.0	:17	:45	:22	:45	2:25	4:00
99.8	:17	:45	:22	:45	3:10	4:30

(1) Stimulative effect of CO_2 more pronounced in mixtures with methyl formate and ethylene oxide.

(2) Concentrations of CO_2 in excess of amount to give maximum increase in insecticidal efficiency may materially lower the toxicity of gaseous mixtures.

(3) Maximum insecticidal effect of methyl formate is achieved with a 40% concentration of CO_2; of ethylene oxide with a 20% concentration of CO_2; of methyl bromide with a 10% concentration of CO_2.

VIII) Comparison of absorption ratios (in presence of flour) and boiling points of several commonly used fumigants. The LC_{50} values for Tribolium confusum adults, exposed in the presence or absence of flour as absorbent are also given. Exposure at 25°C, 760 mmHg: 1013

Fumigant	LC_{50} (mg/l) (No Absorbent)	LC_{50} (mg/l) (In Presence Of Flour)	Absorption Ratio	B.P. (°C)
Methyl bromide	10.2	21	2	4.5
Ethylene oxide	15.5	96	6	11
Hydrocyanic acid	—	—	2	26
Methyl formate	18	78	4	32
Carbon disulfide	64	147	2.5	46
Ethyl formate	22	90	4	54

VIII) Comparison of absorption ratios (in presence of flour) and boiling points of several commonly used fumigants. The LC_{50} values for Tribolium confusum adults, exposed in the presence or absence of flour as absorbent are also given. Exposure at 25°C, 760 mmHg: 1013

Fumigant	LC_{50} (mg/l) (No Absorbent)	LC_{50} (mg/l) (In Presence Of Flour)	Absorption Ratio	B.P. (°C)
Ethylene dichloride	46	240	5	84
Propylene dichloride	45	235	5	97
Chloropicrin	3.9	35.5	9	112
Tetrachlorethylene	54	440	8	120
Methyl thiocyanate	1.4	14	10	130

IX) Toxicity of several fumigants and fumigant mixtures to some stored products insects, exposed at various depths in containers of shelled corn in 5 pound lots, at 30°C, 27 lb lots at 19-26°C: 2605

a) LC_{50}, LC_{95}, $LC_{99.99}$ values for Sitophilus oryzae (adult) exposed to two fumigants and 1 fumigant mixture for 24 hrs. at 30°C in empty space fumigation are given for comparison below:

Fumigant	LC_{50}		LC_{95}		$LC_{99.99}$	
	cc/l	mg/l	cc/l	mg/l	cc/l	mg/l
Carbon tetrachloride	.04 ± .002**	64	.052	83	.065	104
Ethylene dichloride	.023 ± .002**	29	.036	45	.053	67
$CCl_4 + (CH_2)_2Cl_2$*	.024 ± .002**	32	.040	56	.067	90

*Standard mixture. **Confidence limits 19 chances in 20(95%)

b) Fumigation in shelled corn (5 lb lots):

Fumigant	Insect	Exposure (Hrs)	Position In Container	LC_{50} (cc/5 lb corn)	LC_{95} (cc/5 lb corn)
Carbon tetrachloride	Sitophilus oryzae	24	Top	0.171	0.229
" "	" "	"	Bottom	.160	.236
" "	Tribolium castaneum	"	Top	.136	.174
" "	" "	"	Bottom	.129	.164
" "	" "	72	Top	.204	.298
" "	" "	"	Bottom	.178	.280
" "	" "	168	Top	.165	.199
" "	" "	"	Bottom	.157	.193
Carbon tetrachloride	Oryzaephilus surinamensis	24	Top	.150	.214
" "	" "	"	Bottom	.136	.191
Ethylene dichloride	Sitophilus oryzae	24	Top	.259	.426
" "	" "	"	Bottom	.287	.388
" "	Tribolium castaneum	72	Top	.163	.240
" "	" "	"	Bottom	.162	.277
" "	" "	168	Top	.153	.183
" "	" "	"	Bottom	.161	.209
" "	Oryzaephilus surinamensis	24	Top	.152	.346
" "	" "	"	Bottom	.153	.344
$CCl_4 + (CH_2)_2 Cl_2$ Standard Mixture	Tribolium castaneum	24	Top	.247	.370
$CCl_4 + (CH_2)_2 Cl_2$ Standard Mixture	" "	"	Bottom	.250	.316

c) Fumigation in 27 lb lots of shelled corn at 19-26°C:

Fumigant	Insect	Exposure (Hrs)	Dosage			% Mortality At			
			cc/27 lb	cc/5 lb	gal/1000 bu	Overspace	Top	Middle	Bottom
Carbon tetrachloride	Tribolium castaneum	72	0.93	0.17	0.51	96.7	100	100	100
"	"	"	1.08	.20	.59	100	100	100	100
"	"	"	1.4	.26	.77	100	100	100	100
Ethylene dichloride	"	"	.93	.17	.51	8.3	13.1	46.9	49.8
"	"	"	1.08	.20	.59	67.3	64.7	92.2	86.4
"	"	"	1.4	.26	.77	87.9	82.2	96.2	98.1
Carbon tetrachloride	Sitophilus oryzae	72	2.0	.37	1.1	97.8	96.7	98.5	96.0
"	"	24	3.0	.56	1.64	97.4	96.6	99.3	98.8
"	"	24	4.0	.74	2.19	99.2	99.8	99.5	99.8
Ethylene dichloride	"	72	2.0	.37	1.1	94.5	95.6	98.5	95.2
"	"	24	3.0	.56	1.64	100	100	100	100
"	"	24	4.0	.74	2.19	100	99.7	99.6	100
$CCl_4 + (CH_2)_2 Cl_2$ (std.mix.)	"	24	2.0	.37	1.1	95.9	96.9	92.0	95.1
"	"	24	3.0	.56	1.64	94.8	97.8	100	99.9
"	"	24	4.0	.74	2.19	100	100	99.7	100

d) Fumigations with various mixtures in 5 lb lots shelled corn, exposure 24 hrs at 30°C:

Mixture	% By Volume	Insect	Position	LC50 (cc/5 lb)	LC95 (cc/5 lb)
Carbon disulfide + carbon tetrachloride	80 : 20	*Tribolium castaneum*	Top	.062	.085
" "	"	" "	Bottom	.064	.084
" "	50 : 50	" "	Top	.080	.129
" "	"	" "	Bottom	.076	.110
" "	20 : 80	" "	Top	.129	.202
" "	"	" "	Bottom	.124	.182
CS_2 + DNE* + CCl_4	5 : 5 : 90	" "	Top	.159	.226
"	"	" "	Bottom	.141	.206
"	20 : 0 : 80	*Oryzaephilus surinamensis*	Top	.171	.227
"	"	" "	Bottom	.162	.206
"	15 : 5 : 80	" "	Top	.106	.133
"	"	" "	Bottom	.104	.127
"	10 : 10 : 80	" "	Top	.063	.091
"	"	" "	Bottom	.062	.078
"	5 : 15 : 80	" "	Top	.038	.059
"	"	" "	Bottom	.043	.061
"	0 : 20 : 80	" "	Top	.030	.042
"	"	" "	Bottom	.033	.049
β-MeCl** + DNE* + CCl_4	5 : 5 : 90	*T. castaneum*	Top	.124	.174
"	"	"	Bottom	.119	.147

* = 1, 1-Dichloro - 1 - nitroethane; **= β - Methylallyl chloride

e) Effectiveness of various fumigants, as indicated by LC_{50} and LC_{95}, for several species exposed in 5 lb lots of shelled corn at 30°C:

Fumigant	Insect	Exposure (Hrs)	Position	LC50 (cc/5 lb corn)	LC95 (cc/5 lb corn)
Carbon disulfide	*Tribolium castaneum*	24	Top	.055	.083
"	"	"	Bottom	.057	.081
"	"	72	Top	.041	.049
"	"	"	Bottom	.040	.049
"	*Oryzaephilus surinamensis*	24	Top	.067	.091
"	"	"	Bottom	.067	.090
Propylene dichloride	*Tribolium castaneum*	24	Top	.187	.229
"	"	"	Bottom	.193	.254
"	*Oryzaephilus surinamensis*	"	Top	.191	.284
"	"	"	Bottom	—	—
Trichloroethylene	"	"	Top	.231	.397
"	"	"	Bottom	.218	.379
"	*Sitophilus oryzae*	"	Top	.207	.327
"	"	"	Bottom	.188	.324
Isocrotyl chloride	"	"	Top	.173	.269
Isopropyl formate	"	"	Top	.110	.164
"	"	"	Bottom	.104	.145
2-Chlorobutene-2	"	"	Top	.241	.322
"	"	"	Bottom	.233	.313
Methylisopropenyl ketone	"	"	Top	.023	.032
"	"	"	Bottom	.044	.061
Allyl chloride	"	"	Bottom	.049	.067
"	"	"	Top	—	—
1, 1, 2- Trichloroethane	"	"	Top	—	—
"	"	"	Bottom	.134	.244

f) Relative toxicity of various fumigants for *Tribolium confusum* (adult), *Sitophilus granarius* (adult), exposed for 24 hrs, at 80°F, at various depths in whole grain wheat in 28 liter cans, 14.5 in. high, 12.5 in. in diameter, containing 30 lbs wheat at a depth of 8 in., 6.5 in. free space above wheat. 2009

(1) Preliminary remarks:

In fumigation of grains for control of pests consideration must be given to:

(a) Relative toxicity of fumigant to the insect in question.
(b) Diffusion of the fumigant through the material to be treated.
(c) Adsorption (or sorption) capacity of the material, which constitutes a force in opposition to free diffusion.
(d) The sorption capacity of a material must be satisfied before a constant gas concentration can be maintained in surrounding spaces.

(e) As example: The LC_{50} of ethylene dichloride in presence of wheat is 2 times that in empty flask fumigation; the LC_{50} in presence of flour is ca. 8 times that in empty flask fumigation. Ethylene dichloride is 2 times as toxic as carbon tetrachloride in empty space fumigation but in presence of dry corn the difference disappears because of sorption and the two fumigants are ca. equi-toxic.

(f) Molecular weight is not the controlling factor in diffusion speed. Other factors may override, for instance, methyl bromide (mol. wgt. 95) and carbon disulfide (mol. wgt. 76) diffuse through bulk commodities more rapidly than hydrogen cyanide (mol. wgt. 27).

(2) Table (N.B. mg/l÷ 16 = $lb/1000\ ft^3$)

Fumigant	B.P. (°C)	Mol. Wgt.	Depth	T. confusum LC_{50} ←(mg/l)→	T. confusum LC_{95}	S. granarius LC_{50} ←(mg/l)→	S. granarius LC_{95}
Acrylonitrile	78-79	53	Surface	4.6	6.6	<2.6	<2.6
			2 in	8.2	13.6	2.6	4.0
			5.5 in	13.8	19.0	4.0	6.8
Carbon disulfide	46	76	Surface	29.8	43.0	23.8	32.5
			2 in	30.5	43.9	27.6	40.1
			5.5 in	34.5	54.0	29.7	43.0
Carbon tetrachloride	76-77	154	Surface	55.0	110	93	230
			2 in	55.0	110	90	210
			5.5 in	55.0	90	90	200
1,1-Dichloro-1-nitroethane	124	144	Surface	7.9	13.2	4.9	9.8
			2 in	15.5	22.5	7.3	12.2
			5.5 in	17.3	30.1	11.1	21.7
Ethylene chlorobromide	107-108	143	Surface	4.5	7.6	6.6	15.9
			2 in	5.5	20.4	11.5	22.8
			5.5 in	19.0	28.0	16.7	39.1
Ethylene dibromide	132	188	Surface	<7.8	<7.8	<7.8	18
			2 in	<7.8	32	9	24
			5.5 in	34	56	30	60
Ethylene dichloride	84	99	Surface	26	51	67.3	155
			2 in	40.1	75	83.5	>200
			5.5 in	54.4	111	114	>200
Ethylene oxide	11	44	Surface	16.1	23.1	8.2	12.2
			2 in	19	27.6	9	12.6
			5.5 in	22.7	30	10.4	14.3
Hydrogen cyanide	26	27	Surface	<2.5	<2.5	<2.5	31
			2 in	5.9	12.3	7.6	36.4
			5.5 in	16	39	9.6	60.4
Methylallyl chloride	72	91	Surface	7.2	14.2	6.0	12.0
			2 in	9	22	8.5	14
			5.5 in	11	29.5	9.5	15
Methyl bromide	3.6	95	Surface	4.1	5.3	2.3	3.4
			2 in	3.8	4.5	2.4	3.7
			5.5 in	3.8	4.2	2.5	3.9
Acrylonitrile + CCl_4(1:1)	—		Surface	11	18	5	9.8
			2 in	12.5	21	10	19
			5.5 in	20.2	36	12	19
Ethylene chlorobromide + CCl_4(5:95)	—		Surface	27.9	52	30	80
			2 in	28.2	51.8	40	85
			5.5 in	32	68.1	52	94
" " " (10:90)	—		Surface	18.1	38.3	26	50
			2 in	20	52.1	30	64
			5.5 in	33.9	77	43	80
Ethylene dibromide + CCl_4 (5:95)	—		Surface	28.7	42	25.8	47.2
			2 in	31	58	37	69
			5.5	42.7	70	44.2	113.9
Ethylene dichloride + CCl_4 3:1			Surface	21.1	47	63	>190
			2 in	28.1	56.7	72.8	>190
			5.5 in	29.8	59.5	81.5	>190

(3) Dosages (in order of effectiveness) of various fumigants required for 95% mortality at the least effective level (5.5 in. depth) in whole grain wheat of Tribolium confusum (adults), 24 hrs exposure at 80°F, other conditions as in the preceding table (2): 2009

Fumigant	mg/l	cc/0.5 Bushel Wheat
Methyl bromide	5.3*	0.09
Acrylonitrile	19	.67

(3) Dosages (in order of effectiveness) of various fumigants required for 95% mortality at the least effective level (5.5 in. depth) in whole grain wheat of Tribolium confusum (adults), 24 hrs exposure at 80°F, other conditions as in the preceding table (2): 2009

Fumigant	mg/l	cc/1/2 Bushel Wheat
Ethylene chlorobromide	28	.46
Methylallyl chloride	29.5	.89
Ethylene oxide	30	.95
1,1- Dichloro-1-nitroethane	30.1	.59
Hydrogen chloride	39	1.6
Carbon disulfide	54	1.2
Ethylene dibromide	56	.72
Carbon tetrachloride	110*	1.90
Ethylene dichloride	111	2.5
Acrylonitrile 50% + CCl_4 50%	36	.84
Ethylene dichloride 75%+ CCl_4 25%	59.5	1.25
Ethylene chlorobromide 5% + CCl_4 95%	68.1	1.3
Ethylene dibromide 5% + CCl_4 95%	70	1.2
Ethylene chlorobromide 10% + CCl_4 90%	77	1.35
As above, but in order of effectiveness for Sitophilus granarius (adult)		
Methyl bromide	3.9	0.06
Acrylonitrile	6.8	.24
Ethylene oxide	14.3	.45
Methylallyl chloride	15.0	.45
1,1- Dichloro-1-nitroethane	21.7	.43
Ethylene chlorobromide	39.1	.65
Carbon disulfide	43	.95
Ethylene dibromide	60	.77
Hydrogen cyanide	60.4	2.5
Ethylene dichloride	>200	>4.46
Carbon tetrachloride	230 *	4.04
Acrylonitrile 50% + CCl_4 50%	19	.44
Ethylene chlorobromide 10% + CCl_4 90%	80	1.4
" " 5% + " 95%	94	1.65
Ethylene dibromide 5% + CCl_4 95%	>113.9	>2
Ethylene dichloride 75% + CCl_4 25%	>190	>4

*Least effective at the surface of the grain.

g) Sorption by, and penetration through, patent flour of certain fumigants. Surface exposure, 25°C, to fumigant in air at 200 mg/l, standard pressure: 3013

Fumigant	B.P.(°C)	mg Sorbed After 5 Hrs Exposure	Sorption Ratio	mg Fumigant Passed Through In 24 Hrs.	Penetration Ratio
Carbon disulfide	46	10.9	1 (Standard)	154.6	1 (Standard)
Methyl acetate	57.5	68.5	6.3	108.2	.70
Carbon tetrachloride	76.7	14.7	1.3	119.7	.78
Ethylene dichloride	84	41.0	3.8	111.3	.72
Trichloroethylene	87.1	25.6	2.3	95.8	.62
Propylene dichloride	96	34.1	3.1	94.8	.61
Chloropicrin	112	78.3	7.2	65.1	.42
Tetrachloroethylene	120	113.7	10.4	57.6	.37

X) Post-fumigation effect by a sorbed fumigant: HCN, and ethylene oxide, retained by sorption in tobacco, exert a post-fumigant effect even after removal from the fumigation chamber and air washing of the tobacco. 2592

(1) Test insect: Lasioderma serricorne (larva).

(2) Baled tobacco, exposed 4 hrs, at 59°-62°F, absolute pressure 0.16-0.38 inches, air-washed twice after 4 hr exposure. Fumigant: HCN 4.3 and 5 lb per 1000 ft^3:

Period Of Exposure Of Test Insect	Average % Mortality At Designated Depth In Tobacco				
	$1\frac{1}{4}$ in.	$3\frac{1}{4}$ in.	$5\frac{1}{4}$ in.	$7\frac{1}{4}$ in.	$9\frac{1}{4}$ in.
24 hr post fumigation	98.3	88.6	73.7	69.7	69.7
Removed from tobacco after 4 hr exp.	86.3	66.9	65.1	57.1	58.3
48 hr post fumigation	100	96.0	97.3	92.0	82.7
Removed from tobacco after 4 hr exp.	97.3	66.7	69.3	73.3	70.7
67 hr post fumigation	100	98.7	94.7	88.0	86.7
Removed from tobacco after 4 hr exp.	84	66.7	50.7	56.0	58.7

(2) Baled tobacco, exposed 4 hrs, at 59°-62°F, absolute pressure 0.16-0.38 inches, air washed twice after 4 hr exposure. Fumigant: HCN 4.3 and 5 lb per 1000 ft^3:

As above save: Fumigant = ethylene oxide + CO_2 mixture 58.7 lbs per 1000 ft^3 (4.9 lbs per 1000 lbs tobacco), absolute pressure = 0.86 to 1.0 inch; 83°-89°F

Period Of Exposure Of Test Insect	Average % Mortality At Designated Depth In Tobacco				
	$1\frac{1}{4}$ in.	$3\frac{1}{4}$ in.	$5\frac{1}{4}$ in.	$7\frac{1}{4}$ in.	$9\frac{1}{4}$ in.
24 Hrs Post Fumigation	97.0	83.3	90.2	88.7	84.6
Removed from tobacco after 4 hr exp.	88.9	81.2	77.4	82.0	81.5
48 hr post fumigation	97.0	93.4	80.2	83.7	84.2
Removed from tobacco after 4 hr exp.	86.3	77.4	55.9	73.9	69.7
72 hr post fumigation	100	94.0	92.9	89.0	89.0
Removed from tobacco after 4 hr exp.	96.0	94.6	91.0	84.0	81.8

a) Residual action of sorbed fumigants of low vapor pressure; duration of toxic effect in open vessels of patent flour, as tested against Tribolium confusum adults: 2853

(1) Flour, 375g, depth 3 inches, separated by gauze from 2 cc fumigant on blotting paper; exposure 4 days;

(2) Insects exposed below surface of flour and near surface of flour:

Fumigant	V.P. (mmHg$^{25°C}$)	50-100% Kill (days)	100% Kill (days)
Acrylonitrile	117.0	2	1
Chloropicrin	24.0	2	2
Ethylene dibromide	13.5	20	12
Dichloroethyl ether	3.0	28	0
Hexachloropropene	.3	172	66
sym-Heptachloropropane	.1	176	112 Still 100% effective at experiment's end.
Lindane (γ-BHC) as 40% sol in acetone)	2.1×10^{-5}	0	0 (Experiment ended at 50 days)

XI) Practical dosages of fumigants suggested for use in steel storage bins to control such stored products insects as: Sitophilus oryzae, S. granarius, Rhizopertha dominica, Plodia interpunctella, Sitotraga cerealella, etc.: 609

Fumigant	Dosage (Gallons/1000 Bushels)	
	Wheat	Corn (Maize)
Carbon disulfide	1	1.5
Carbon tetrachloride	3	4
$CS_2 + CCl_4$ (1 : 4)	2	5
Chloropicrin 2 lb + CCl_4 to make 1 gallon	1.5	1
Ethylene dichloride + CCl_4 (3 : 1)	4	5
1,1-Dichloro-1-nitroethane 2 lb + CCl_4 to make 1 gallon	1.5	1
β-Methylallyl chloride 1 lb + CCl_4 to make 1 gallon	2	2
Ethylene dichloride + CCl_4 (3 : 1) + 10% methyl bromide	2	2
Ethylene dichloride + methyl bromide (9 : 1)	2	2
CCl_4 + methyl bromide (9 : 1)	2	2
Methyl chloride + methyl bromide (9 : 1)	2	2
Propylene dichloride + methyl bromide (9 : 1)	2	2
Propylene dichloride + CCl_4 (3 : 1) + 10% methyl bromide	2	2

XII) Relative susceptibility to fumigants of various insect species, and life-cycle phases within species. Relative toxicities of various fumigants to diverse insect species at various temperatures:

a) Relative susceptibility of 6 insect species exposed 5 hrs, at 25°C, in empty fumigation flasks to 3 common fumigants. 156

Insect	Chloropicrin LC_{50} (mg/l)	Carbon disulfide LC_{50} (mg/l)	Ethylene dichloride LC_{50} (mg/l)
Tribolium confusum	4.6	61	37.5
Tribolium castaneum	2.4	28	—
Sitophilus granarius	5.0	40	138
Sitophilus oryzae	2.0	26	31
Oryzaephilus surinamensis	1.4	34	—
Bruchus obtectus	<1.3	22	72

b) Relative (comparative) toxicity of 4 fumigants for Tribolium confusum (adult), exposed 5 hrs at various temperatures, empty flask fumigation: 156

Temperature (°C)	Chloropicrin (mg/l)		Carbon disulfide (mg/l)		Ethylene dichloride (mg/l)		CCl_4 (mg/l)	
	LC_{50}	LC_{99}	LC_{50}	LC_{99}	LC_{50}	LC_{99}	LC_{50}	LC_{99}
35	1.8	2.4	32	40	40	60	75	225
30	2.8	5.0	44	68	39	57	125	490

Temperature (°C)	Chloropicrin (mg/l)		Carbon disulfide (mg/l)		Ethylene dichloride (mg/l)		CCl_4 (mg/l)	
	LC_{50}	LC_{99}	LC_{50}	LC_{99}	LC_{50}	LC_{99}	LC_{50}	LC_{99}
25	4.6	7.0	61	91	38	73	185	405
20	5.9	9.9	76	108	37	87	225	564
15	7.1	12.3	86	140	60	120	230	589
10	11.5	15.7	154	280	80	140	250	535
5	7.8	15.4	140	270	62	138	—	—
0	4.6	8.6	—	—	48	78	—	—

c) Relative susceptibility to fumigants of various life cycle stages of insects, as determined by several workers:

Insect	Fumigant	Susceptibility In Decreasing Order.	
Cimex	Hydrogen cyanide	egg > young nymph > adult > old nymph	412
Cimex	Sulfur dioxide	young nymph > adult > old nymph > egg	412
Ephestia	Carbon disulfide	adult > larva > pupa	412
Lyctus	Hydrogen cyanide	larva > adult > pupa	412
Tribolium	Carbon disulfide	larva > adult > pupa > egg	2003
Tribolium	Chloropicrin	larva > adult > pupa > egg	2003
Tribolium	Ethylene oxide	egg > larva > adult > pupa	2003
Tribolium	Hydrogen cyanide	egg > larva > adult > pupa	1231

XIII) Toxicity values of various fumigants, recorded by various workers, for insects tested by different exposures and under diverse conditions:

a) Toxicity to certain insects of various substances in use as, or suggested for, insect fumigants. Exposures 5 hrs. at 25°C in empty fumigation flasks. Adult insects. 156

(1) LC_{99} values calculated from the dose mortality curves as suggested in the general statements at the beginning of this section see equation under (1) (c):

Fumigant	B.P.(°C)	Tribolium confusum		Sitophilus granarius		Sitophilus oryzae	
		LC_{50} (mg/l)	LC_{99}	LC_{50} (mg/l)	LC_{99}	LC_{50} (mg/l)	LC_{99}
Hydrogen cyanide	26	0.6	1.1	5.8	11.4	—	—
Chloropicrin	112	4.6	7.0	5.0	21.0	2.0	15.2
Sulfur dioxide	-10	5.7	10.7	5.7	11.3	17	46.9
Ethylene oxide	11	18	31.2	5.6	11.2	5.7	7.5
Carbon disulfide	46	61	91	40	66.0	26	40.0
Methyl formate	32	23.5	37.5	20	36.0	—	—
Ethyl formate	54	24.5	32.5	29	49.0	17.5	35.5
Methyl bromide	5	11.2	14.4	7.4	8.4	4.0	6.2
Methyl acetate	57	82	130	88	129.0	63	81
Ethyl acetate	77	83	123	86	178.0	49	71
Ethylene dichloride	84	37.5	73	138	246	31	137
Propylene dichloride	97	40	98	118	234	44	132
tert-Butyl alcohol	83	43	67	73	109	32	60
Trichloroethylene	87	108	268	335	405	196	316
Carbon tetrachloride	76	185	405	360	859	160	559
Furoyl chloride	176	9	16	2.6	—	—	—
Propylene oxide	35	32	52	25	41	—	—
Acetyl chloride	52	3.6	5.6	—	—	—	—
Propionyl chloride	80	4.1	8.3	5.0	14.0	—	—
Thionyl chloride	79	2.0	3.8	3.0	9.0	—	—
α,β-Dichloroethyl ether	140	2.1	3.1	1.7	4.7	—	—
β,β-Dichloroethyl ether	178	1.8	3.5	1.7	3.7	—	—
Chloromethyl ether	58-60	10.2	10.3	—	—	—	—
sym-Dichloromethyl ether	100-108	3.3	14.2	—	—	—	—
Methylene chloride	40.5-42	82	182	—	—	—	—
sym-Dichloroethylene	58-61	154	303	—	—	—	—
Tetrachloroethylene	119-121	55	99	—	—	—	—
1,1,2-Trichloroethane	110-117	38.5	60.5	—	—	—	—
Chloroform	61	157	267	240	660	—	—
Methyl thiocyanate	130-131	1.6	2.6	3.5	5.7	—	—
Ethyl thioacetate	115-116	45	63	20	34	—	—

b) Toxicities of some widely used fumigants tested against 8 species of stored products insects. Treatment in 100 ft^3 gas-tight fumatoria at 70°F; insects held in empty flasks during exposure; mortality counts made 4 days after treatment; adult insects (imagines): 2005

b) Toxicities of some widely used fumigants tested against 8 species of stored products insects. Treatment in 100 ft^3 gas-tight fumatoria at 70°F; insects held in empty flasks during exposure; mortality counts made 4 days after treatment; adult insects (imagines): 2005

Fumigant	Insect	LC_{50} (mg/l)		LC_{95} (mg/l)	
		2 Hrs Exposure	6 Hrs Exposure	2 Hrs Exposure	6 Hrs Exposure
Acrylonitrile	Acanthoscelides obtectus	3	1.1	5.5	2
"	Oryzaephilus surinamensis	3.5	0.8	6.5	1.4
"	Rhizopertha dominica	2.5	0.8	4	1.4
"	Sitophilus granarius	4.5	2	8	2.9
"	Sitophilus oryzae	2.5	1	6.5	1.8
"	Stegobium paniceum	3	1.7	7	2.5
"	Tribolium confusum	6.5	3	11	4.9
"	Zabrotes pectoralis	2	1.4	4	2.1
Carbon disulfide	A. obtectus	54	29	90	43
"	O. surinamensis	119	40	>179	68
"	R. dominica	72	31	108	49
"	S. granarius	103	43	149	65
"	S. oryzae	48	36	80	50
"	S. paniceum	110	42	168	62
"	T. confusum	>179	75	>179	103
"	Z. pectoralis	84	46	106	64
Chloropicrin	A. obtectus	1.5	< 1.5	2.8	< 1.5
"	O. surinamensis	3.5	< 1.5	10	3.2
"	R. dominica	4.5	< 1.5	10.5	2.6
"	S. granarius	16	3.4	34.5	8
"	S. oryzae	7.5	< 1.5	28	3.9
"	S. paniceum	5.5	1.9	16	5.4
"	T. confusum	23.5	6.4	31	13
"	Z. pectoralis	1.7	< 1.5	2.9	< 1.5
Ethylene chlorobromide	A. obtectus	26	22	51	28
"	O. surinamensis	12	6	35	18
"	R. dominica	15.5	6	37	19
"	S. granarius	23	3.6	48	16
"	S. oryzae	31	7.5	53	20.5
"	S. paniceum	32	14	53	25
"	T. confusum	14.5	5	26.5	18
"	Z. pectoralis	24	11.5	40	21
Ethylene dibromide	A. obtectus	21	10.2	35	16.8
"	O. surinamensis	1.8	0.9	6.5	3.2
"	R. dominica	3.8	3	10.5	6.2
"	S. granarius	14	3	29	12
"	S. oryzae	14	2.6	31	10
"	S. paniceum	6.5	2.8	11	6.4
"	T. confusum	12.5	3.4	21	7.2
"	Z. pectoralis	5	2.2	9.5	5.2
Ethylene dichloride	A. obtectus	127	49	186	83
"	O. surinamensis	122	39	230	77
"	R. dominica	137	65	228	106
"	S. granarius	>271	127	>271	>135
"	S. oryzae	166	66	>271	123
"	S. paniceum	161	77	242	128
"	T. confusum	132	53	226	84
"	Z. pectoralis	52	26	92	48
Ethylene oxide	A. obtectus	13.5	10.5	39	30
"	O. surinamensis	14.5	4	29.5	10
"	R. dominica	14.7	6.2	33	11.6
"	S. granarius	21	13.5	31	24.5
"	S. oryzae	14	5.4	28.5	10.4
"	S. paniceum	14	9	22.5	13
"	T. confusum	> 40	27.5	> 40	37.5
"	Z. pectoralis	12.7	6	20.5	11
Hydrogen cyanide	A. obtectus	1.5	0.9	4.5	2.7
"	O. surinamensis	0.6	< 0.4	1.4	1.2
"	R. dominica	1.2	0.8	4.4	2.6
"	S. granarius	23	4.6	29	9.9
"	S. oryzae	20	2.8	26	5.9

Fumigant	Insect	LC$_{50}$ (mg/l) 2 Hrs Exposure	LC$_{50}$ (mg/l) 6 Hrs Exposure	LC$_{95}$ (mg/l) 2 Hrs Exposure	LC$_{95}$ (mg/l) 6 Hrs Exposure
Hydrogen cyanide	*S. paniceum*	0.5	< 0.4	1	0.7
"	*T. confusum*	1	0.8	2.2	1.6
"	*Z. pectoralis*	1.4	1	4.4	2.7
Methyallyl chloride	*A. obtectus*	36	18	58	28
"	*O. surinamensis*	43	19	65	29
Methyallyl chloride	*R. dominica*	68	25	96	41
"	*S. granarius*	65	25	87	45
"	*S. oryzae*	41	12	58	27
"	*S. paniceum*	47	27	77	39
"	*T. confusum*	58	27	75	41
"	*Z. pectoralis*	14	10	26	18
Methyl bromide	*A. obtectus*	9	4.2	22	6.6
"	*O. surinamensis*	17	4.4	28	6.8
"	*R. dominica*	11	3.4	19	5.5
"	*S. granarius*	18.5	4.8	27	6.8
"	*S. oryzae*	9.5	3.6	15	6.1
"	*S. paniceum*	15.5	4.4	27	6.7
"	*T. confusum*	32.5	9.2	44	13.8
"	*Z. pectoralis*	10.5	3.5	15.5	6

c) Substances tested as fumigants, selected from 309 aliphatic compounds tested for toxicity for *Sitophilus oryzae* adults. 2670

(1) 24 hrs exposure, at ca. 25°C, in 500 cc flasks containing 200 g (ca. 250 cc) grain wheat; mortality recorded at 48 hrs after treatment. Insects in contact only with the vapour phase of the tested compounds:

(2) Most effective of the 309 tested aliphatic compounds. LD$_{100}$ here indicates the minimum dosage applied at which 100% mortality ensued:

Compound	LD$_{100}$ (mg/l)	Compound	LD$_{100}$ (mg/l)
Ethyl mercaptan	<17	Allyl bromide	<28
Isopropyl thiocyanate	<19	2-Bromoethyl acetate	<30
Ethyl isothiocyanate	<20	Methyl bromoacetate	<30
Allyl isothiocyanate	<20	Ethyl bromoacetate	<30
Methyl disulfide	<21	n-Propyl iodide	<35
tert.-Butyl bromide	<24	Allyl iodide	<37
Epichlorhydrin	<24	Ethyl iodide	<39
2-Chloroethyl ether	<24	Methyl iodide	<46
2-Bromoethyl ethyl ether	<27	Methylene iodide	<67

Other tested compounds which proved lethal in dosages <100 mg/l:

Compound	LD$_{100}$ (mg/l)	Compound	LD$_{100}$ (mg/l)
Ethylene oxide	20	Diisopropylamine	72
Isobutyl mercaptan	33	Methyl chloroacetate	73
tert.-Butyl chloride	34	Isobutyraldehyde	79
Isobutyl formate	35	tert-Butyl alcohol	79
Allyl formate	38	Ethyl disulfide	79
Methyl formate	39	Isocapronitrile	81
2-Chloroethyl acetate	47	n-Propyl bromide	81
n-Propyl mercaptan	48	Methyl-n-butyl ketone	83
Mesityl oxide	52	Ethyl-1-bromopropionate	84
Isopropyl formate	53	Isoamyl mercaptan	84
Propylene oxide	54	Ethyl isobutyrate	87
Carbon tetrabromide	60	Isobutyl acetate	87
Isobutyl iodide	64	Ethylene dibromide	87
sec.-Butyl iodide	64	Isoamyl nitrite	87
Methyl butyl carbinol	64	Propylene chlorhydrin	89
Methyl isobutyl ketone	64	n-Propyl acetate	89
Methyl thiocyanate	64	Diacetyl monomethoxime	90
tert.-Amyl alcohol	65	α-Methyl hydroxylamine	90
Dimethyl n-propyl carbinol	66	Ethyl orthoformate	90
n-Butyl mercaptan	67	n-Butyl nitrite	91
Isopropyl iodide	68	Ethyl chloroacetate	93
Isoamyl formate	70	Methyl n-propyl ketone	97
Ethyl formate	72	n-Butyl iodide	97
n-Propyl formate	72	Ethyl thiocyanate	100

Some compounds whose LD_{100} was in excess of 100 mg/l:

Compound	LD_{100} (mg/l)	Compound	LD_{100} (mg/l)
Ethyl bromide	172	n-Butyl chloride	265
Carbon tetrachloride	638	Trichloroethylene	650
Trichloroethane	404	Tetrachloroethylene	649
sym-Tetrachloroethane	384	Acetonitrile	392 maximum tested; gave 90% Kill
Pentachloroethane	342	Propionitrile	235
n-Propyl chloride	445	n-Butyronitrile	238
Isopropyl chloride	430	n-Valeronitrile	224
Propylene chloride	140	Nitroethane	211

d) Chemical constitution and fumigant toxicity of some N-heterocyclic compounds. Tested against *Tribolium confusum* (adult), fumigated in empty containers at 5 hrs. exposures: 1798

Compound	LC_{50} (mg/l)	LC_{90} (mg/l)
Pyridine	7.2	8.35
2-Methyl-pyridine	10.1	13.0
2-Ethyl-pyridine	11.3	14.3
2-n-Propyl-pyridine	4.8	5.8
2-Isopropyl-pyridine	14.5	—
2-n-Butyl-pyridine	6.4	8.7
2-n-Amyl-pyridine	10.8	Not at saturation.
2-n-Hexyl-pyridine	Not toxic to this degree at saturation.	
2-mixed Hexyl-pyridine	" " "	
2-n-Heptyl-pyridine	" " "	
2-n-Octyl-pyridine	" " "	
2-(3-Octyl)-pyridine	" " "	
2-(2-Methyloctyl)-pyridine	" " "	
2-(6-Undecyl)-pyridine	" " "	
2-(mixed-Undecyl)-pyridine	" " "	
3-Methyl-pyridine	5.4	
4-Ethyl-pyridine	7.2	
4-n-Propyl-pyridine	3.5	
4-Isopropyl-pyridine	3.8	
4-n-Butyl-pyridine	4.4 (erratic)	
4-n-Amyl-pyridine	8.0	
4-(3-Pentyl)-pyridine	29.0	
4-n-Hexyl-pyridine	Not toxic to this degree at saturation.	
4-mixed-Hexyl-pyridine	" " "	
2-Methyl-4-methyl-pyridine	9.0	
2-Methyl-5-methyl-pyridine	6.6	
2-Methyl-6-methyl-pyridine	6.5	
2-Ethyl-6-methyl-pyridine	9.0	
2-Butyl-6-methyl-pyridine	4.5	
2-Amyl-6-methyl-pyridine	Not toxic to this degree at saturation.	
2-Hexyl-6-methyl-pyridine	" " "	
2-Ethanol pyridine	35.0	
2-n-Hexyl-piperidine	11.0	
4-n-Amyl-piperidine	7.6 (erratic)	
Quinoline	60.0	

For Comparison The Following Common Fumigants:

Carbon disulfide	55.0
Methyl acetate	82.0
Ethyl acetate	90.0
$\beta,-\beta'$-Dichloroethyl ether	1.3
Ethylene dichloride	19.0
Carbon tetrachloride	66.0

e) Effect of point of attachment of the alkyl side-chain on the toxicity of alkyl-pyridines: 1798

Chain Length	Concentration (mg/l)	% Mortality With		Concentration mg/l	% Mortality With	
		2-Substituted Compound	4-Substituted		2-Substituted	4-Substituted
		Oncopeltus fasciatus			*Tribolium confusum*	
Ethyl-	2	10	100	5	2	6
n-Propyl	2	100	100	5	65	83
iso-Propyl	2	0	100	5	1	37
n-Butyl	1	65	100	5	26	74
n-Amyl	2	85	100	5	2	23
n-Hexyl	2	15	40	5	2	0
mixed-Hexyl	2	0	45	5	6	0

e) Effect of point of attachment of the alkyl side-chain on the toxicity of alkyl-pyridines: 1798

Position And Chain Length	Test Arthropod	Concentration (mg/l)	% Kill By Normal Chain Compound	% Kill By Branched Chain Compound
2-Propyl	Tetranychus telarius	3	35	5
"	Oncopeltus fasciatus	2	100	0
"	Tribolium confusum	5	65	1
4-Propyl	O. fasciatus	0.5	25	5
"	O. fasciatus	1	35	10
"	T. confusum	2	16	0
"	T. confusum	5	83	37
4-Amyl	T. confusum	10	52	12
2-Hexyl	T. telarius	3	41	30
"	O. fasciatus	2	15	0
"	O. fasciatus	3	20	10
"	T. confusum	5	2	6
"	T. confusum	40	12	14
4-Hexyl	O. fasciatus	2	40	45
"	O. fasciatus	3	0	75
"	T. confusum	10	0	17
2-Octyl	O. fasciatus	5	35	70
"	O. fasciatus	10	55	35
"	T. confusum	2	1	1

XIV) Miscellaneous tables: Toxic effect of various fumigants on particular insects of economic importance:

a) Fumigants for Tenebrioides mauritanicus (the Cadelle beetle), effects of: Exposure 24 hrs., at 30°C, in 5 lb lots of shelled corn (maize). Adult insects: 2603

Fumigant	LC_{50}		LC_{95}	
	cc/5 lb corn	g/5 lb corn	cc/5 lb corn	g/5 lb corn
1,1-Dichloro-1-nitroethane	0.019	0.027	0.024	0.034
Ethylene dibromide	.2	.043	.036	.078
Carbon disulfide	.102	.129	.111	.104
Methyl bromide + CCl_4 10:90 v/v	.120	.191	.161	.256
β-Methylallyl chloride	.131	.121	.208	.192
" "	.108	.100	.191	.177
Carbon tetrachloride	.276	.438	.455	.723
1,1,2-Trichloroethane	.352	.508	.566	.817
Ethylene dichloride	.467	.585	.903	1.135

b) Toxicity values of certain fumigants for Limonius californicus and their relative toxicity compared to carbon disulfide: 1957

Fumigant	LC_{50} (mg/l) (Values Rounded)	Approximate LC_{100} (mg/l)	Relative Toxicity CS_2 = 1
Carbon disulfide	31.5	51	1.0
Methyl cyanide	55.8	86	0.56
Ethylene chloride	24.5	39.3	1.3
Ethyl formate	16.65	28.3	1.9
Diethyl carbinol	15.7	25.6	2.0
Methyl formate	12.5	23	2.5
Pyridine	5.9	15	5.3
α,β-Dichloroethyl ether	3.4	7.4	9.2
β,β'-Dichloroethyl ether	0.9	2.5	35
Epichlorhydrin	0.8	2.4	39.8
Crotonaldehyde	0.74	1.1-1.3	42.4
Chloropicrin	0.7	0.86	45.9
Ethylene chlorohydrin	0.24	0.6-0.8	131.9
Allyl isothiocyanate	0.16	0.21-0.24	192.9

c) Fumigants vs. certain fumigation resistant insects, namely: Larvae of Tineola bisselliella, Attagenus piceus, Anthrenus vorax: 2670

(1) Seventeen best fumigants, and fumigant mixtures, from standpoints of effectiveness, cheapness, availability, freedom from fire hazard. Exposures 24 hrs. in vials buried in "overstuffed" furniture. Lowest dosage (lb/1000 ft^3) yielding 100% kill in 24 hrs.

Compound	Parts By Volume	Compound	Pts By Vol.	Temp(°F)	LD_{100} 24 Hrs lb/1000 ft^3
Carbon tetrachloride		——	—	85	30
Carbon tetrachloride	1	Ethylene chloride	3	85	6
Carbon tetrachloride	1	Ethylene chloride	3	65	12

(1) Seventeen best fumigants, and fumigant mixtures, from standpoints of effectiveness, cheapness, availability, freedom from fire hazard. Exposures 24 hrs. in vials buried in "overstuffed" furniture. Lowest dosage (lb/1000 ft^3) yielding 100% kill in 24 hrs.

Compound	Parts By Volume	Compound	Pts By Vol.	Temp (°F)	LD_{100} 24 Hrs. lb/1000 ft^3
Carbon tetrachloride	7	tert-Butyl chloride	3	83	12
Trichloroethylene	—	——	—	83	12
Tetrachloroethylene	—	——	—	85	30
Carbon tetrachloride	3	Ethyl iodide	1	85	5
Carbon tetrachloride	7	tert-Butyl alcohol	3	85	20
Ethylene oxide	—	——	—	75	1
Carbon tetrachloride	7	n-Propyl formate	3	85	11
Carbon tetrachloride	3	Isopropyl formate	1	85	14
Carbon tetrachloride	3	sec-Butyl formate	2	85	8
Carbon tetrachloride	3	Isobutyl formate	2	85	9
Carbon tetrachloride	3	Isoamyl formate	2	85	7
Carbon tetrachloride	7	Isopropyl acetate	3	83	15
Methyl monochloroacetate	—	——	—	83	1
Ethyl monochloroacetate	—	——	—	83	2
Isopropyl monochloroacetate	—	——	—	83	1.5
Carbon tetrachloride	1	Diethyl carbonate	1	83	30$^+$
Carbon disulfide				80	1.5

d) Fumigants vs. Dacus orientalis (Oriental fruit fly) eggs (naked, 23-26 hrs. old) and larvae (3rd instar): 255
(1) Exposure 2 hr. at 71°-80°F, in empty fumigation vessels.

Fumigant	LC_{50}-(mg/l)-LC_{95} Eggs		LC_{50}-(mg/l)-LC_{95} Larvae	
Acetonitrile	44	75	> 82.4	—
Chloroacetonitrile	1.2	1.5	< 1.3	< 1.3
Acrylonitrile	1.2	1.6	< 1.2	1.6
Acrylonitrile + CCl_4 50:50	3.7	11	1.7	4.9
Carbon disulfide	53	92	56	89
Carbon tetrachloride	>167.8	—	>167.8	—
Methyl iodide	< 2.9	< 2.9	< 2.9	4.2
Methyl thiocyanate	2.7	8.5	< 1.4	< 1.4
1-Bromo-2-chloroethane	< 2.2	< 2.2	< 2.2	2.3
Ethylene dibromide	< 2.9	< 2.9	< 2.9	< 2.9
Chlorobromopropene	5.9	8.7	2.0	3.1
1,3-Dichloropropene	3.9	8.7	6.0	13.5
Ethyl chloroacetate	6.2	13.5	1.4	3.6
Methyl bromide	15.0	24.5	9.2	18.5
Methyl formate	65	110	—	—
Hydrogen cyanide	10	26	1.3	2.8
Propylene oxide	> 87.4	—	18.5	28.0
Ethylene oxide	6.2	12.0	8.7	17.0
Ethylene dichloride	2.3	5.9	38	120.0
Ethyl formate	>104	—	—	—
1,1,1-Trichloroethane	28	69	<139	—
sym-Tetrachloroethane	25	68	20	43
1,1-Dichloro-1-nitroethane	24	60	< 1.9	< 1.9
Allyl chloride	71	105	70	> 98.6
Allyl bromide	15	24	1.8	7.5

e) Fumigants for Dacus dorsalis naked eggs and larvae: Compounds which at dosages of <50 mg/l, after exposures of 2 hrs. at 75° ± 2°F, yielded 95% mortality (here designated LC_{95}) within 48 hrs. after treatment. 1537

Compound		LC_{95} (mg/l) Eggs	Larvae
Butane, 1-chloro-4-iodo- in CCl_4	2%	0.7	0.3
" " "	10%	.3	< .9
Methane, diiodo-		.6	.7
Heptane, 1-iodo-		< .8	< .8
Hexane, 1-iodo-		<1.1	< .7
Isothiocyanic acid, ethyl ester		4.0	1.2
Ethane, iodo-		7.0	.3
Propene, 3-iodo		7.2	.8

e) Fumigants for Dacus dorsalis naked eggs and larvae: Compounds which at dosages of <50 mg/l, after exposures of 2 hrs at 75° ± 2°F, yield 95% mortality (here designated LC$_{95}$) within 48 hrs. after treatment. 1537

Compound	LC$_{95}$ (mg/l)	
	Eggs	Larvae
2-Butane, 1, 4-dichloro-	6.1	3.3
Cyclohexane, iodo	7.6	2.0
Epibromohydrin	8.9	4.0
Butane, 1, 2-dibromo-	8.7	7.8
Propane, 1,2-dibromo-	18	1.8
Crotonaldehyde	11	10
Propane, 1,3-dibromo-	5.5	18
Pentane, 1-iodo-	<3.9	20
Toluene, α-bromo	13	11
Butane, 1-iodo	<4.1	22
Epichlorhydrin	24	3.5
Cyclopentane, bromo	16	14
Propane, 1-iodo	5.5	35
Butane, 1-iodo-3-methyl-	14	31
Butane, 1-bromo-3-chloro-	29	19
Butylamine	13	38
Cyclopentane, chloro-	31	24
Propane, 1-iodo-2-methyl-	16	45
Propane, 2-bromo-1-chloro-	39	28
Xylene, α-chloro-	27	43
Propane, 1-bromo-3-chloro-	27	44
Butane, 2-iodo-	36	41

f) Fumigants which have decided toxicity for Aonidiella (= Chrysomphalus) aurantii: 669

Fumigant	Conditions	Results
Hydrogen cyanide	1.5 mg/l 25 min exp at 25°C	Survival of 15-30%
Isobutyl mercaptan	Saturation 25 min exp at 25°C	" 3.2% (resistant stage)
"	2 cc/50 gal 25 min exp at 26°C	" 89 % (")
n-Butyl thiocyanate	3.8 mg/l + HCN 1.5 mg/l 25 min exp at 25°C	" 2.7% (")
"	Saturation 25 min exp at 25°C	" 71 % (")
Chloropicrin	8.8 mg/l + 1.5 mg/l HCN 25 min exp at 25°C	" 30 % (")
"	10 mg/l 25 min exp at 25°C	" 25 % (damage to lemon fruit)
"	9.5 mg/l + 5% CO$_2$ exp 25 min at 25°C	" 8 % (")
Ethyl acrylate	10 mg/l + HCN 1.5 mg/l exp 25 min at 25°C	" 3 % (")
Ethylene oxide	0.8% v/v + 0.9 mg/l HCN exp 30 min at 25°C	" 16 % (")
"	2.4% v/v 45 min exp at 25°C	100% kill (")
Ethyl thiocyanate	3.5 mg/l 25 min exp at 25°C	Survival of 38 % (all stages)
"	4.8 mg/l " "	100% kill (")
Ethyl isothiocyanate	6.6 mg/l + HCN 1.5 mg/l 25 min exp at 25°C	Survival of 3 % (great experimental
"	7.6 " " " "	" 21 % variability)
Hydrogen sulfide	25% v/v 25 min exp at 25°C	" 1 %
Methyl acetate	Saturation 45 min exp at 25°C	" 2 % (severe damage to lemon)
"	14 mg/l + HCN 1.5 mg/l 25 min exp at 25°C	" 23 %
Methyl propionate	Saturation exp 25 min at 25°C	" 0.2%
"	As spray 4 cc/50 gallon container 25°C	" 93 %
"	11 mg/l + 1.5 mg/l HCN (last 25 min) 30 min exp at 25°C	" 1.8%
Methyl thiocyanate	6.6 " " " "	" 0.9%
"	10 mg/l 25 min exp at 25°C	" 0.3% (all stages)
Methyl isothiocyanate	7.4 mg/l (1:1 $\bar{c}$ Me thiocyanate) 25 min exp at 25°C	" 0.8% (")
Oxalyl chloride	Sprayed at 3 cc/50 gallon container 25 min exp at 25°C	" 19 %
n-Propyl chlorocarbonate	Saturation exp 25 min at 25°C	" 11 %
"	12.2 mg/l " "	" 78 %
Isopropyl ether	Saturation exp 25 min at 25°C	" 21 %
Isopropyl thiocyanate	6.3 mg/l " "	" 40 % (all stages)

Allyl isothiocyanate was only moderately toxic as were: Acetylacetone, acrolein, arsenic trichloride, bromoform, bromopicrin, carbon disulfide, carbon dioxide, crotonaldehyde, ethyl bromoacetate, ethyl nitrite, o-fluorotoluene, formic acid, gasoline, methylamine, methyl chlorocarbonate, methylene chloride, α-methyl hydroxylamine, methyl nitrite, methyl selenocyanate, methyl sulfide, perchloromethyl mercaptan, piperidine, n-propyl ether, n-propyl-n-propionate, sulfur dioxide, trichloroethylene, vinyl acetate.

g) Fumigants and the disinfestation of nursery stock harboring San José scale (Aspidiotus perniciosus): 222

Fumigant	[c] Concentration (g/m^3)	[t] Fumigation Time (hr)	[c]x[t]	% Mortality
Hydrogen cyanide	5	0.05	.25	98.1
"	5	.1	.5	100

g) Fumigants and the disinfestation of nursery stock harboring San José scale (*Aspidiotus perniciosus*): 222

Fumigant	[c] Concentration (g/m^3)	[t] Fumigation Time (hr)	[c]x[t]	% Mortality
Hydrogen cyanide	5	.15	.75	100
"	14	.118	.25	92.4
"	14	.035	.5	99.8
"	14	.071	1	100
"	2.5	.1	.25	96.4
"	2.5	.2	.5	99.6
"	2.5	.4	1	99.8
"	2.5	.8	2	100
Ethylene oxide	15	.2	3	51.9
"	15	.4	6	63.7
"	15	.66	10	64.2
"	15	1.0	15	72.4
"	15	1.33	20	80.9
"	15	1.66	25	99.0
"	15	2	30	100
Methyl bromide	25	.1	2.5	60.7
"	25	.2	5	49.7
"	25	.3	7.5	97.6
"	25	.4	10	99.6
"	25	.8	20	99.0
"	25	1.0	25	100
"	25	1.2	30	100
Phosphine	2	.25	.5	24.9
"	2	.5	1.0	45.2
"	2	1.0	2	83.6
"	2	2	4	80.5
"	2	4	8	98.0
"	2	5	10	97.4
"	2	7.5	15	99.0
"	2	10	20	96.4
"	2	12.5	25	99.8
"	2	15	30	100

h) Median lethal concentrations (LC_{50}) of various fumigants for wireworms, *Limonius canus* and *L. californicus*, tested in 1 liter flasks containing 500 g soil, exposure 5 hrs. at 77°F: 1958

Fumigant	LC_{50} (mg/l)	Fumigant	LC_{50} (mg/l)
Allyl isothiocyanate	2.33	Methyl bromide	5.9
Ethyl isothiocyanate	3.2	Methyl disulfide	18.8
Allyl bromide	4.2	Allyl chloride	23.5
Chloropicrin	4.8	Epichlorohydrin	67.2
Methyl iodide	5.2	Carbon disulfide	68.2
Allyl iodide	5.5	Allyl formate	102.2

Compounds, in descending order of toxicity, whose LC_{50} values ranged from 100-200 mg/l: Allyl formate, β-bromoethyl ethyl ether, iso-butyl valerate, butyraldehyde, ethyl iodide, ethyl isobutyrate, propylene oxide, methyl bromoacetate, sec-butyl iodide, n-propyl mercaptan, ethyl bromoacetate, ethyl caproate, trichloroethylene, methyl formate, n-butyl mercaptan, isobutyl iodide, β-bromoethyl acetate, isobutyl benzoate, butyl butyrate, cuminic aldehyde, propyl butyrate, n-propyl iodide, methyl-n-butyrate.

Compounds whose LC_{50} values ranged from 200-300 mg/l: Ethyl phenylacetate, isopropyl thiocyanate, bromoform, β-chloroethyl acetate, ethylene chloride, isopropyl formate, amyl propionate, isobutyl mercaptan, propylene chloride, mesityl oxide, β,-β'-dichloroethyl ether, dichloroethylene, ethyl thiocyanate.

Compounds with LC_{50} values of 300 mg/l or >: Ethyl bromide, propyl propionate, amyl formate, isobutyl acetate, tetrahydronaphthalene, pinene, methyl caprylate, ethylene chlorohydrin, phenyl butyl ketone, bromostyrol.

i) Fumigant toxicities for *Cimex lectularius*, exposed for 5 hrs., at 25°C, in 12 liter glass flasks, various life-cycle stages: 2622

(1)

Fumigant	Approximate LC_{95}-LC_{100} (mg/l)		
	Older Nymphs	Adults	Eggs
Hydrogen cyanide	0.4	< 0.4	< 0.4
Acrylonitrile	3-4	< 2.5	2
Chloracetonitrile	3-4	< 3	< 3
Chloropicrin	5-6	3	< 2.75

i) Fumigant toxicities for *Cimex lectularius*, exposed for 5 hrs., at 25°C, in 12 liter glass flasks, various life-cycle stages: 2622

(1)

Fumigant	Approximate LC_{95}-LC_{100} (mg/l)		
	Older Nymphs	Adults	Eggs
α,β-Dichloroethyl ether	5-6	5-6	> 6
Acrylonitrile + CCl_4 1:1	7.5	6-7.5	6
1,1-Dichloro-1-nitroethane	8	< 8	< 8
Methyl bromide	9	< 7	< 7
Dichloroacetonitrile	10	< 8	< 8
Trichloroacetonitrile	11	8	< 8
Ethylene oxide	14	6-10	< 2
Methyl allyl chloride	25-30	<25	<25
Ethyl formate	30	25-30	<25
Ethylene oxide + ethylene dichloride 1:3	35	25-30	<25
sym-Tetrachloroethane	35	35	25
Carbon disulfide	37.5	<30	30
Ethylene dichloride	>50	>50	>50
Ethylene dichloride + CCl_4 3:1	>50	>50	>50
Carbon tetrachloride	>50	>50	>50
Trichloroethylene	>50	>50	>50

(2) % Mortality of *Cimex lectularius*, exposed under various conditions to fumigant dosages of 20 mg/l for 5 hrs., at 77°F, 760 mmHg; ON = older nymphs, A = adults, E = eggs. 2622

Fumigant	% Mortality for Cimex Wrapped In								
	Cotton Batting			Woolen Blanket			Woolen Blanket In Barracks Bag		
	ON	A	E	ON	A	E	ON	A	E
Methyl bromide	100	100	100	100	100	100	100	100	100
Chloropicrin	"	"	"	"	"	"	"	"	"
Hydrogen cyanide	"	"	"	"	"	"	61.3	96.7	"
Acrylonitrile + CCl_4 1:1	"	"	"	92.8	"	"	20	25	20.5
Trichloroacetonitrile	94.5	97.5	96.8	75	"	"	64	89.4	98.3
1,1-Dichloro-1-nitroethane	76.6	97.5	78	66.7	97.9	84.3	31.5	67.4	54.3
Ethylene oxide	37.7	—	—	17.8	—	—	24.2	—	—
Chloroacetonitrile	30.6	75	—	1.9	7.3	—	14.8	14.0	—

j) Comparative toxicity of various fumigants for *Tribolium confusum*; exposures 5 hrs., static fumigation at 25°C, 50-75 insects per test, 6-8 tests per fumigant; mortality data taken 20-21 days after treatment and adjusted for normal death rate: 2629

Fumigant	Approximate concentration (mg/l)		Remarks
	For 50% Kills	For 95% Kills	
Chloroacetonitrile	< 2	< 3	Death in 6 hr.
Acrylonitrile	> 2	< 3	Death in 6 hr.
Methyl bromide	ca 8	ca 11	
1,1-Dichloro-1-nitropropane	8	11	
1,1-Dichloro-1-nitroethane	9	12	
Ethylene dichloride*	6	12	Delayed; mortality over 20 day period.
Ethylene Cl_2 + CCl_4 3:1	9	14	
Methylallyl chloride	12	19	
Methylallyl bromide	14	—	
Ethylene oxide	< 20	< 25	
Carbon disulfide	56	100	
Ethyl bromide	> 150	< 200	

*A delayed mortality over the first 10 days and much longer, 40%-60% being killed between 10-20 days with only a slight increase in mortality 20-40 days after treatment. Viable eggs may be laid during this time; prevention: Increase dosage.

k) Toxicity of certain vapors for *Sitophilus* (= *Calandra*) *granarius*: exposures of 5 hrs., at 25°C in 5-6 l fumigation vessels (empty) 50 adult insects per trial: 984

Substance	V.P. At 25°C (mmHg)	LC_{50} (mg/l)	Substance	V.P. At 25°C	LC_{50} (mg/l)
Pentane	511	897	Propyl bromide	133	133
Hexane	151	353	Butyl bromide	40	66
Heptane	45.6	137	Amyl bromide	13.2	35
Decane	1.6	12	iso-Propyl bromide	211	516
iso-Pentane	700	1020	iso-Butyl bromide	60.2	130

k) Toxicity of certain vapors for *Sitophilus* (= *Calandra*) *granarius*: exposures of 5 hrs., at 25°C in 5-6 l fumigation vessels (empty) 50 adult insects per trial: 984

Substance	V.P. At 25°C (mmHg)	LC$_{50}$ (mg/l)	Substance	V.P. At 25°C	LC$_{50}$ (mg/l)
Cyclohexane	97	180	iso-Amyl bromide	17.9	45
Benzene	93.9	210	Methyl iodide	402	2
Toluene	28.5	96	Ethyl iodide	133	11
Ethyl benzene	9.6	50	Propyl iodide	44	5.9
Propyl benzene	3.5	30	Butyl iodide	14	5
Butyl benzene	1.2	<50% at saturation	Amyl iodide	4.4	4.6
o-Xylene	6.64	31	iso-Propyl iodide	67	65
p-Xylene	8.87	48	Methylene chloride	429	380
Mesitylene	2.9	25	Chloroform	199	250
pseudo-Cumene	1.7	<50% kill at saturation	Carbon tetrachloride	114.5	275
Methyl chloride	4200	166	Methylene bromide	45	90
Ethyl chloride	1170	1124	Bromoform	5.4	16
Propyl chloride	339	428	Ethylene dichloride	78	98.9
Butyl chloride	107	200	sym-Tetrachloroethane	6.95	15.4
Amyl chloride	32	73	asym.-Tetrachloroethane	14	33.4
iso-Propyl chloride	521	740	β-Trichloroethane	24.5	53
iso-Amyl chloride	44	93	Ethylidene chloride	225	380
tert-Butyl chloride	300	82	Methyl chloroform	131.2	290
Methyl bromide	1580	3.3	Pentachloroethane	4.6	16.3
Ethyl bromide	465	205	Hexachloroethane	.44	<50% kill at saturation
1,3-Dichloropropane	27	59	Methyl propyl ketone	39	29
Ethylene dibromide	11	.66	Methyl formate	6245	15
trans-Dichlorethylene	320	425	Ethyl formate	255	35
cis-Dichlorethylene	224	298	Propyl formate	83	28
Trichlorethylene	73	190	iso-Propyl formate	140	34
Perchlorethylene	19	91	Methyl acetate	210	84
Fluorobenzene	76	180	Ethyl acetate	94	56
Chlorbenzene	11.8	45	Propyl acetate	33	45
Brombenzene	4.2	20	Butyl acetate	11.2	41
Methanol	124	100	iso-Propyl acetate	60	90
Ethanol	58.6	85	Acetaldehyde	930	35
Propanol	20.1	50	Propionaldehyde	350	25
Butanol	6.78	30	Butyraldehyde	110	50
Amyl alcohol	2.5	<50% kill at saturation	Valeric aldehyde	33	21
iso-Propanol	44.4	76	Ammonia	7500	4.4
Acetone	230	110	Diethylamine	250	12
Methyl ethyl ketone	93.2	50	Triethylamine	66	24
Diethyl ketone	36.6	34	n-Propylamine	27	15
n-Butylamine	110	20	Carbon disulfide	360	30
iso-Butylamine	151	45			

l) Relative resistance of 4 insect forms to three common fumigants. Exposures 5 hrs., at 25°C (in case of SO_2 at 20°C): 412

Insect	Ethylene oxide LC$_{99}$ (mg/l)	Hydrogen cyanide LC$_{99}$ (mg/l)	Sulfur dioxide LC$_{99}$(mg/l)
Sitophilus granarius	8.4	14.0	8.3
S. oryzae	4.1	12.0	10.8
Tribolium castaneum	27.0	.36	9.7
Cimex lectularius	12.3	.17	5.9

105

INSECTICIDE SPRAYS; BEHAVIOR OF DROPLETS OF DIFFERENT SIZES

1) Size of droplets, and number of droplets deposited per unit area by distributing uniformly over a 1 acre surface 1 gallon of liquid: 2534

Droplet Diameter (μ)	Droplet Volume (μ^3)	Droplets per mm^2	Droplets per inch^2
1	0.52	1,780,125	—
2	4.2	222,516	—
3	14.8	65,930	—
4	33.6	27,814	—
5	65.6	14,242	—
6	113.4	8,241	—
7	180	5,197	—
8	269	3,476	—
10	525	1,780	1,148,000
12	907	1,030	—
13.5	1289	725	—
15	1772	527	—
17.5	2814	332	—
18	3062	305	—
20	4200	222	143,190
24	7257	129	—
25	7442	125	80,625
30	14,175	66	42,570
35	22,507	41.5	26,767
40	33,600	27.8	17,931
45	47,838	19.5	12,577
50	65,520	14.3	9,224
55	87,343	10.6	6,837
60	113,400	8.2	5,289
70	180,007	5.2	3,354
80	268,800	3.5	2,157
90	382,725	2.44	1,574
100	525,000	1.78	1,164
110	699,000	1.33	856
120	907,000	1.03	664
130	1,153,000	.81	530
140	1,440,000	.65	425
150	1,771,000	.53	347
160	2,150,000	.43	277
170	2,579,000	.36	232
180	3,061,000	.30	194
190	3,600,000	.26	168
200	4,200,000	.22	142
220	5,590,000	.17	111
240	7,257,000	.12	78
260	9,227,000	.10	65
280	11,528,000	.08	52
300	14,175,000	.066	43
400		.028	18
500		.014	9
1000		.0018	1.1

2) Time required for droplets of specific gravity 1.0 to fall 50 feet in ordinary still air at 23°C: 2534

Droplet Diameter (μ)	Time
200	13 sec.
100	51 sec.

2) Time required for droplets of specific gravity 1.0 to fall 50 feet in ordinary still air at 23°C: (continued) 2534

Droplet Diameter (μ)	Time
80	1.3 min.
50	3.4 min.
40	5.2 min.
20	21.0 min.
10	1.4 hr.
5	5.5 hr.
1	5.0 days

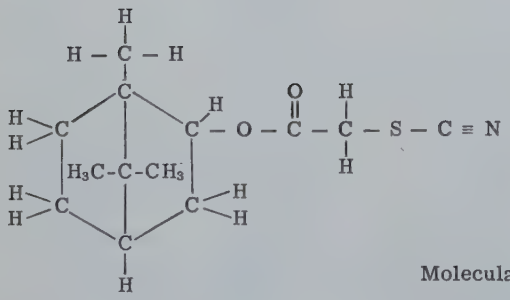
3) Distance travelled by a droplet of specific gravity 1.0, 100 $\mu\mu$ in diameter, by drift, while falling 50 feet in air moving parallel to ground: 2534

Air Movement (miles/hour)	Feet Drifted
0.25	22
0.5	45
1	87
2	175
3	265
4	348
5	435
10	765

106

ISOBORNYL THIOCYANOACETATE

(Thanite®; Terpinyl thiocyanoacetate.)



Molecular weight 253.36

GENERAL

[Refs.: 2506, 292, 130, 1236, 636, 353, 2231]

Thanite® is an insecticide which belongs to a general group often referred to generically as the organic thiocyanates. Thanite® is prepared by the conversion of pine oil or turpentine fractions to secondary alcohols which by reaction with monochloroacetic acid are, in turn, converted to alkyl halogen esters. These last, by reaction with sodium thiocyanate, yield the technical product Thanite®, of which the isobornyl ester comprises ca. 82%. Like the insecticides of its group, Thanite® is a swiftly-acting contact toxicant for insects, with a rapid "knock-down" action. It has been, thus, widely used as an ingredient of fly and mosquito space sprays either to replace or supplement the pyrethrins, with which it synergizes. Thanite® has also found employment as a livestock spray. Thanite® is too hazardous, by reason of high phytotoxicity, to be used on plants in the manner in which some organic thiocyanates may be employed for control of aphids and their eggs, leaf hoppers, thrips, mealy bugs, or white flies. Thanite® is, for all practical purposes, virtually non-toxic for higher animals although it is irritating to eyes, mucous surfaces, and skin. These latter disadvantages are unfortunate in view of the potency of Thanite® as a pediculicide.

PHYSICAL, CHEMICAL

The technical product is a yellow oily liquid (a mixture of ca. 82% isobornyl thiocyanoacetate and ca. 18% of other active terpene esters); odor is turpentine-like; $d^{25°}_{4°}$ 1.1465; $n^{25°}_{D}$ 1.512; v.p. 0.06 mm Hg at 95°C; virtually insoluble in water; very soluble in alcohol, benzene, chloroform, ether, and in various oils and fats; flash point 180°F (open cup); stable under ordinary conditions of storage; corrosive toward galvanized iron.

a) Formulated ordinarily as kerosene or petroleum oil solutions, up to 10%; to 5% in water base emulsions.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage	Remarks	
Rat	or	LD_0	0.2-1 cc/k	Undiluted; as single dose.	129
Rat	or	LD_{50}	1000 mg/k		1951
Rat	or	LD_{50}	6 cc/k		2506
Guinea Pig	or	LD_{50}	2 cc/k		2506
Rabbit	ct	LD_{50}	6.0 cc/k	Single dermal application.	1952

2) Chronic toxicity and other effects; higher animals:

a) Rats: Tolerated up to 0.6 cc per k daily in 6 month feeding tests. 129

b) Man: Inhalation of "heavy mist" of 5% Thanite® in kerosene 30 minutes per day for 10 days gave no effects of adverse nature. 129

c) Animals tolerated 8 hours exposure per day for 6 months, in inhalation experiments, with but minor effects. 129

d) Solutions are irritating to skin and eyes. Exposure over a time produces a thickening of the exposed skin. No irritation is reported from use of 5% Thanite® in an inert powder diluent on the skin. 129

e) General symptoms of organic thiocyanate intoxication include: Restlessness, profound depression, cyanosis, dyspnoea, tonic convulsions; death, in fatal cases, by respiratory paralysis. 1951

f) Absorption of a lethal dose brings quick death. Pathology, in fatal poisonings, includes fibrinous pneumonitis of a monocytic nature and liver vacuolation. 2078

g) Stated to be dangerous when applied to skin in doses of 500 mg per k. 3201

h) Toxicity for all animals tested may be generalized as follows: Oral LD_{50} 1000 mg/k; chronic oral exposure for symptoms or death 600 ppm in the diet; danger level by skin inunction 5000 mg/k; principal pathology in tissues is hepatic. 1951 353

3) Phytotoxicity:

a) Too phytotoxic to be used directly on plants.

4) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Cimex lectularius (adult)	Contact Spray	LC_{50}(% conc.)	75	As spray in P_{31} white oil at 0.36 mg spray/cm².	413
Pediculus humanus corporis (adult)	Contact Spray	LC_{50}(% conc.)	3.2	As spray in P_{31} white oil at 0.36 mg spray/cm².	413
Pediculus humanus corporis (egg)	Contact Spray	LC_{15}(% conc.)	> 50% conc.	Spray (as above) yields only 15% mortality.	413
Periplaneta americana ♂	Topical	LD_0	3.5 mg/g	Av. wgt. of insects = .9/.7-1.15)g.	2219
Periplaneta americana ♀	Topical	LD_0	> 7 mg/g	Non-toxic for ♀♀ by topical route.	2219
Periplaneta americana ♂	Topical	LD_{50}	4.8 mg/g	Av. wgt. of insects = .9 (.7-1.15)g.	2219
Periplaneta americana ♂	Topical	LD_{100}	ca.6.0 mg/g		2219
Periplaneta americana ♂♀	inj	LD_0	0.2 mg/g	Av. wgt. insects ♂ = .9 (.7 -1.15)g.	2219
Periplaneta americana ♂♀	inj	LD_{50}	0.3 mg/g	Av. wgt. insects ♀ = 1.3 (1.0-1.9)g.	2219
Periplaneta americana ♂♀	inj	LD_{100}	0.45 mg/g		2219
Musca domestica (adult)	Contact Spray	LC	1.75% w/w	Yielded 36% kill in Peet-Grady tests.	1236

5) Comparative toxicity, for insects, of Thanite® and other insecticides:

a) Insects: Pediculus humanus corporis, Cimex lectularius, Periplaneta americana.

2219,41

Insecticide	LC_{50} (%), Contact Spray In P_{31} Oil At 0.36 mg/cm²		Periplaneta (mg/g)											
			Topical						Injection					
			LD_0		LD_{50}		LD_{100}		LD_0		LD_{50}		LD_{100}	
	Pediculus	Cimex	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Isobornyl thiocyanoacetate(Thanite®)	3.2	75.0	3.5	7+	4.8	—	6.0	—	0.2		0.3		0.45	
β-Butoxy-β′-thiocyanodiethyl ether*	1.5	4.0	0.36	0.56	0.66	1.26	1.36	2.3	0.1	0.12	0.15	0.2	0.2	0.4
Lethane®, special	2.4	12.5	—	—	—	—	—	—	—	—	—	—	—	—
β-Thiocyanoethyl laurate	8.1	32.0	—	—	—	—	—	—	—	—	—	—	—	—
Lauryl thiocyanate**	6.0	19.5	—	—	—	—	—	—	0.4		0.9		1.5	
Bis-ethyl xanthogen	6.2	75.0	—	—	—	—	—	—	—	—	—	—	—	—
Benzyl benzoate	21.0	75.0	—	—	—	—	—	—	—	—	—	—	—	—
Lindane	0.016	0.051	—	—	—	—	—	—	—	—	—	—	—	—
DDT	0.030	0.56	—	—	—	—	—	—	0.002	0.01	0.008	0.02	0.02	0.04
Pyrethrins***	0.038	0.026	0.002	0.006	0.004	0.009	0.006	0.012	0.001	0.005	0.003	0.008	0.006	0.011

* For Periplaneta as β-butoxy-β′-thiocyanodiethyl ether 50% (Lethane® 384).

** For Periplaneta as Lorol thiocyanate 60% lauryl (93% total thiocyanates mixed).

*** Plus 2% isobutyl undecyleneamide (as synergist) for Pediculus, Cimex.

b) Toxicity for Thanite® and other thiocyanoacetates and related substances, for Musca domestica: 1236

Thiocyanoacetate	% "Knockdown" In				Comments
	2.5 min.	5 min.	7.5 min.	10 min.	
Isobornyl- (Thanite®)	14	42	65	93	Non-irritant.
Methyl-	2	15	37	58	Irritant.
n-Hexyl-	9	56	99	100	Irritant.
Cyclohexyl-	26	47	72	99	Irritant.
2-Ethylhexyl-	14	42	56	84	Slightly irritant.
Capryl-	0	9	23	58	Slightly irritant.
Carvomenthyl-	3	48	64	91	Non-irritant.
Fenchyl-	7	35	59	95	Non-irritant.
Decahydro-2-naphthyl-	7	19	32	51	Non-irritant.
1-Methyl-3-cyclohexyl-n-propyl-	2	13	28	60	Non-irritant.
4-tert.-Butylcyclohexyl-	5	18	27	51	Non-irritant.
Lauryl-	0	0	0	2	Non-irritant.
4-ααβγ-Tetramethyl-n-butylphenyl-	6	15	15	16	Irritant.
Tetrahydrofurfuryl-	0	17	23	25	Very irritant.
1-Methyl-3-(α-tetrahydrofurfuryl-n-propyl-	2	42	61	91	Very irritant.
β,β-di)α-Tetrahydrofurfuryl) diethyl-carbinyl	0	1	6	28	Very irritant.
2-Methoxyethyl-	14	16	27	35	Irritant.
2-Butoxyethyl-	4	32	53	86	Irritant.
2-Caproxyethyl-	5	35	49	88	Slightly irritant.
2-Fenchoxyethyl-	23	46	73	90	Non-irritant.
2-(1-Methyl)-3(α -tetrahydrofurfuryl)-n-propoxy)ethyl-	40	61	78	93	Very irritant.
2-β-Naphthoxyethyl-	0	0	0	5	Irritant.
2-(2-Ethoxyethoxy)-ethyl-	6	12	12	14	Slightly irritant.
Thiocyanoacetone	25	41	69	91	Very irritant.
Thiocyano-4-cyclohexyl butanone-2	1	23	61	90	Irritant
Thiocyanotetrahydroionone	0	0	0	4	Non-irritant.
ω-Thiocyanoacetophenone	49	74	82	98	Very irritant.
ω-Thiocyano-4-methoxyacetophenone	0	2	2	3	Very irritant.
2-Thiocyanocyclohexanone	21	40	47	57	Irritant.
2-Thiocyano-4-tert.-butylcyclohexanone	0	0	0	6	Irritant.
1-Thiocyanoheptene-1	2	4	4	7	Non-irritant.
5-Thiocyano-2,3-dihydropyran	1	3	3	3	Non-irritant.
Ethyl thiocyanofumarate	1	1	1	2	Non-irritant.
4-Methyl-2-hydroxythiazole	1	1	1	2	Non-irritant.
4-Phenyl-2-hydroxythiazole	1	2	2	3	Non-irritant.
Acetone (control)	0	1	1	1	—
Purified kerosene (control)	0	0	0	0	—

Compound	Concentration w/w (%)	% Mortality
Isobornyl thiocyanoacetate	1.75	36
Fenchyl thiocyanoacetate*	1.75	38
Fenchyl thiocyanoacetate*	2.5	62
Fenchyl thiocyanoacetate*	3.25	94
Pyrethrins (standard)	0.1 w/v	38

* Fenchyl thiocyanoacetate is a constant ingredient of technical Thanite®.

(1) Isobornyl thiocyanoacetate (Thanite®) gives extremely rapid "knockdown" of Musca domestica and there is no recovery if the concentration is sufficiently high. DDT (0.1%) + Thanite® (2%) in odorless kerosene as a space spray at rate of 1 cc/m³ from atomizers yielded complete fly control. 636

(2) For the control of Cochliomyia macellaria (larva) in carcasses, Thanite® proved to be among the most effective compounds. 2166

(3) Thanite®, at 25 lbs per acre, yielded effective, but transient, action vs. Eutrombicula alfreddugesi. 2024

6) Pharmacological, pharmacodynamical, physiological, etc., insects: 2600,1422

a) On insects, Thanite® exerts an immediate depressant and profoundly narcotic effect. 2599,1236

b) A selective nerve degeneration (not so marked as with pyrethrins) is evident.

c) The neural lesions in Culex pipiens and Aëdes aegypti (larvae) resemble the lesions produced by pyrethrins. Vacuolization of the nerve elements is marked. Similar manifestations have been reported for Thanite®-intoxicated Musca domestica.

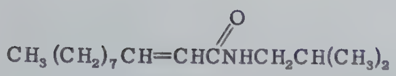
d) On nerve cord choline esterase of Apis and Periplaneta, there is stated to be no effect, although the thiocyanate insecticides are stated to diminish choline esterase(s) activity, and to be potentiated by acetylcholine.

7) Screening test data:

a) Screening tests indicate for Thanite® high activity vs. lice in "knockdown" and mortality; similar high activity vs. ticks and chiggers; moderately high mosquito larvicidal action; moderately high killing action vs. fleas; high action as a dust formulation vs. Blattella germanica.

107

N-ISOBUTYL UNDECYLENEAMIDE (N-Isobutyl hendecenamide; Isobutylamide of Undecylenic acid; IN 930.)



$CH_3(CH_2)_7CH{=}CHC(=O)NHCH_2CH(CH_3)_2$ Molecular weight: 239.39

GENERAL

[Refs.: 2120, 353, 2231, 3037, 3258, 1426, 2012, 700, 1596, 2596, 2468, 2469, 1668, 1672, 1667, 1670, 1669, 655, 1755, 2432, 2017, 314, 3380, 2344.]

A nitrogen substituted amide which (though of low insecticidal activity by itself) has a potent adjuvant, synergistic or potentiating action for pyrethrins when used in kerosene-solution sprays against *Musca domestica*, lice, etc. The synergistic effect is manifested even with N-isobutyl undecyleneamide used as a ''pre-treatment'' for flies, before the application of pyrethrins. Thus, a spray containing 40 mg. of pyrethrins and 420 mg. N-isobutyl undecyleneamide in 100 cc of solvent is superior in killing action vs. *Musca domestica* to a standard solution of pyrethrins at 100 mg per 100 cc.

A consideration of the action of N-isobutyl undecyleneamide involves a general consideration of the problem of synergism in the field of insecticides. A number of references are shown, and attention is drawn to the section, in this work, titled Synergism; Synergists.

Other N-isobutylamides of aliphatic acids have shown insecticidal power when used alone, and some comments on these are included below.

PHYSICAL, CHEMICAL

Produced by allowing castor oil to react with isobutylamine, the product being then pyrolized. A liquid of mild odor; virtually insoluble in water; soluble in various oils. 308

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Apparently of low toxicity for higher animals. 4 cc/k, orally, to rats killed 70% of the subjects in from 20 to 90 minutes. Subcutaneous injections of 7.27 cc/k were tolerated by rats without any overt effects. No evidence of skin irritation was reported. 2120

2) Effects on insects:
   a) Histopathological studies of *Musca domestica* treated with N-isobutyl undecyleneamide have shown distinct effects, notably a lysis of nuclear chromatin in the cells of nerve and associated tissues. Some workers have dismissed these effects as being produced only by concentrations totally outside the range of practical synergistic effect and reproducible by anaeroxia alone. 2432
   b) The synergistic effect of N-isobutyl undecyleneamide remains when such physical variables as droplet size, stabilization of insecticide (pyrethrins), etc., are controlled and eliminated. 2432
   c) The toxicity of pyrethrins is enhanced by a factor of 3 when up to equimolecular proportions of N-isobutyl undecyleneamide are added. Further increase in proportion of N-isobutyl undecyleneamide is ineffective in bringing about additional enhancement of toxicity. 2432
   d) Addition of synergist decreased the mean weight of pyrethrins required to paralyse individual *Aëdes aegypti* from 6.0×10^{-7} to 2.0×10^{-7}, but once a 1:1 molecular ratio was achieved no further decrease in the ''knockdown'' threshold weight of pyrethrins was possible. The toxicity of pyrethrins for *Sitophilus granarius* was also enhanced by a factor of 3. 2432
      (1) A surface complex between synergist and pyrethrin at the peripheral nerve sheath interfaces is suggested—a complex which, by reorientating the pyrethrin molecule, produces a more efficient discharge of nerve resting potential at the interface. Thus, a complex of N-isobutyl undecyleneamide + pyrethrin 3 times as toxic as pyrethrin alone is proposed.
   e) N-isobutyl undecyleneamide showed no synergism with isobornyl thiocyanoacetate which has a pyrethrin-like action on insects. The effect appears limited to the pyrethrins. 1779
   f) Persistence of the synergistic effect when N-isobutyl undecyleneamide is used as a ''pre-treatment'', before pyrethrin application, has already been mentioned. The effect has been noted with *Musca domestica* and *Aëdes aegypti*. 700,3380 2012

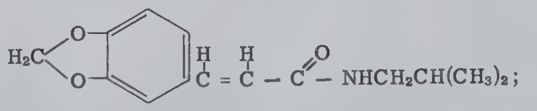
3) Uses:
   a) In addition to its use in pyrethrin sprays for flies, mosquitoes, etc., N-isobutyl undecyleneamide is an ingredient of MYL powder, a pediculicide which contains, in addition, pyrethrins, an antioxidant substance, Phenol-S, and 2,4-dinitroanisole as an ovicide. 409,1833

4) Related substances:

a) Certain synthetics, for example N-isobutyl-2,4-decadienamide and N-isobutyl-2-dodeceneamide give, alone, 3258
rapid paralytic ("knockdown") action but low mortality in treated Musca.

b) Among relatives of N-isobutyl undecyleneamide which are themselves insecticidal, saturation of double 3258
bonds abolishes this action, although in the case of N-isobutyl lauramide synergistic action with pyrethrins persists.

c) Fagaramide, from Fagara xanthoxyloides and F. macrophylla shows the same N-isobutyl carbamyl group 1156
as N-isobutyl undecyleneamide: 1224,3084

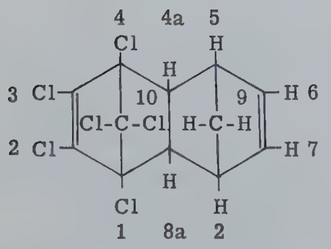


; fagarimide synergises with pyrethrins and at 2 mg/cc + 0.5 mg/cc pyrethrins kills as many flies as a spray with 1 mg/cc pyrethrins alone.

d) Other related substances are: Spilanthol (N-isobutyl-4,6-decadienamide), Pellitorine (N-isobutyl-2,6-de- 2468
cadienamide), N-isobutyl-2,6,8-decatrieneamide, Herculin (N-isobutyl-2,8-dodecadienamide), Scabrin 2469,1668
(N-isobutyl-2,4,8,10,14-octadecapentaenamide or N-isobutyl-2,4,8,12,14-octadecapentaenamide. These 1672,1667
show both insecticidal and/or synergistic action with pyrethrins. 1670,1669,655

108

ISODRIN (1, 2, 3, 4, 10, 10-Hexachloro-1, 4, 4a, 5, 8, 8a-hexahydro-1, 4-endo, endo-5,8-dimethanonaphthalene; Experimental Insecticide 711 (J. Hyman Co.).)



Molecular weight: 364.94

GENERAL

[Refs.: 269, 353, 2231, 2120, 1756, 1757, 1988, 2639, 2640, 2119, 1996]

One of the group of compounds known, among other designations, as the cyclodiene insecticides which, besides isodrin, includes aldrin, chlordane, dieldrin, endrin, heptachlor, toxaphene, q.v., all highly chlorinated cyclic hydrocarbons with an endomethylene bridge in their structure. Isodrin is the endo, endo-isomer of aldrin. By treatment with peracetic acid, isodrin may be converted to an epoxide which is endrin, q.v.. Isodrin may be synthesized by the reaction of hexachlorocyclopentadiene with vinyl chloride, with formation of 1,2,3,4,5,7,7-heptachlorobicyclo-[2,2,1]-2-heptene, which is then treated slowly with cyclopentadiene and heated. The insecticides of the cyclodiene group are potently toxic for many insects and have found extensive employment in control of Orthoptera, cotton, household, soil insects, etc. This group of compounds is of recent introduction, isodrin, for example, having been brought forward as an insecticide of promise in 1951. As the names of several of the group suggest, these insecticides are (save toxaphene) produced by the Diels-Alder diene reaction. Isodrin is not to be used on food or forage crops near harvest.

PHYSICAL, CHEMICAL

Pure: A white crystalline solid; m. p. 240°-242°C (with slow decomposition beginning above 100°C;) virtually insoluble in water; soluble in aromatic and paraffinic solvents, for instance as grams isodrin per 100 cc solvent at 25°C: Acetone 17, benzene 138, carbon tetrachloride 3.3, hexane 7.1, xylene 18.3; stable in alkalis and relatively weak acids; compatible with most of the commonly used agricultural spray materials.

a) Formulated as: 19% emulsifiable concentrate; 25% wettable powder; dusts; emulsifiable concentrate (Canada) 2 lbs per gallon (Imperial).

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) In experimental animals (rat, rabbit, chicken) isodrin is distinctly more toxic than aldrin of which it is a stereoisomer. In rats marked difference in susceptibility of the sexes is evident. Among rats and chickens age differences in susceptibility are apparent. 2824,3122 3128,3120

b) The toxicity of isodrin is comparable with that of endrin, as the toxicities of aldrin and dieldrin are comparable. 3122 3120

c) Saturation of the double bond of isodrin (as in aldrin) reduces toxicity greatly. 3122

d) Isodrin is to be considered highly toxic. 3122

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat (weanling) ♀	or	LD$_{50}$	16.42(12.55-21.48)	In peanut oil as 0.1,.2,.5,1.0% w/v.	3122
Rat (weanling) ♂	or	LD$_{50}$	27.76(23.17-33.25)	" "	3122
Rat (weanling) ♀	or	MLD(est)	7-10	" "	3122
Rat (weanling) ♂	or	MLD(est)	10-16	" "	3122
Rat (6 mo. old) ♀	or	LD$_{50}$	11.74(10.22-13.50)	" "	3122
Rat (6 mo. old) ♂	or	LD$_{50}$	42.06(35.85-49.35)	" "	3122
Rat (6 mo. old) ♀	or	MLD(est)	5-7	" "	3122
Rat (6 mo. old) ♂	or	MLD(est)	24-36	" "	3122
Rabbit (heterogeneous group)	or	MLD(est)	10-16	Preliminary experiments.	3122
Rabbit ♀	or	MLD(est)	3-5	More toxic as 1.0% than as 0.1% w/v sol.	3122
Rabbit	ct	MLD 24 hr	< 94	24 hr dry application to clipped skin under rubber sleeve.	3122
Chicken (7 day old)	or	LD$_{50}$	2.7	In acetone; by gelatin capsule; older birds more resistant.	2824

Results of cutaneous application as dry powder (100 mesh) in 24 hr. contact with clipped and intact skin under rubber sleeve (method of Draize et al.), to rabbits: 3122

No. Animals	Dose (mg/k)	No. Dead/No. Tested	Remarks
3	250	3/3	Death within 34, 41 hours.
3	160	2/3	Death within 42,65 hours.
3	125	2/3	Death in 28.2 hr, 11 days.
3	94	2/3	Death in 32, within 72 hr.

2) Subchronic toxicity:

a) Chickens, receiving 12 ppm isodrin in diet over 42 day period, showed > 90% mortality (endrin > 90% mortality; aldrin, dieldrin 20% mortality at 50 ppm). 2825

(1) Significantly lower weight gains were made by survivors of 6 ppm and 12 ppm isodrin feedings at 7 weeks of age than by controls (female birds).

(2) Food consumption of birds on 12 ppm isodrin was significantly less than among controls.

Isodrin Conc. (ppm)	Mean % Mortality	Mean Wgt. Gain (g) Survivors At 7 Weeks ♂♂	♀♀
12	92.5	No survivors	576.3
6	0	783.2	595.6
3	2.5	784.2	673.3
1.5	0	875.3	702.0
(Controls) 0	0	842.9	703.6
Least Sig. Diff. (5%)		61.5	46.4
Least Sig. Diff. (1%)		—	61.5

3) Comparative toxicity:

a) Comparative toxicity of aldrin, dieldrin, endrin, isodrin for experimental animals. 3122,2824,3128,3120

Animal	Dose	Route	Insecticide; Dosage (mg/k); Spatial Configuration			
			Isodrin endo-endo	Endrin endo-endo	Aldrin endo-exo	Dieldrin endo-exo
Rat ♀ *	LD$_{50}$	or***	16.4 (12.6-21.5)	16.8 (13.0-21.7)	45.9 (35.8-54.2)	38.3 (32.7-44.8)
Rat ♂ *	LD$_{50}$	or***	27.8 (23.2-32.3)	28.8 (16.2-51.2)	49	47
Rabbit	MLD	or***	3-5	5-7	40	35
Chicken**	LD$_{50}$	or****	2.7	3.5	25.5	43
Rabbit	MLD	ct*****	< 94	60-94	600-1250	250-360

* Weanling.
** 7 days old.
*** As solutions in peanut oil.
**** As acetone solution in capsule.
***** As dry powder, 100 mesh, 24 hr. contact, clipped skin under sleeve.

4) Pharmacological, pharmacodynamical, physiological, etc.; higher animals:

a) Rats, receiving LD$_{50}$ (oral): Hypersensitivity to stimulus, alterations of respiratory rate and pattern, convulsions (in 6 mo. old ♀♀ at 13 mg/k, ♂♂ at 55 mg/k). 3122

b) Rabbits, receiving MLD oral: Violent convulsions on dosages as low as 16 mg/k. Weight loss in survivors not great, the loss being recouped. 3122

c) Chickens, receiving LD$_{50}$: Rapid respiration with concomitant convulsions, nervousness, excitability, crouching with dragging movement on keel, rolling on back, violent thrashing movements, compulsive circling movement while lying on side; in some fatal instances death within 5 minutes of exposure to oral LD$_{50}$. 2824

d) Rats, receiving fatal doses: Pathology: Moderate, diffuse degeneration of liver, kidney; slight degenerative changes of heart, brain. 3122

e) Rabbits, receiving fatal oral doses: Pathology: Severe, diffuse degeneration of liver, kidney, heart, brain; in some instances fatty, cytoplasmic vacuolization of hepatic cells of central lobular zone; necrosis of distal, convoluted renal tubules. 3122

f) Rat, Rabbit survivors of LD$_{50}$, MLD oral doses showed no visceral pathology attributable to isodrin exposure. 3122

g) Rabbit, percutaneous administration: Convulsions; in fatal cases diffuse degeneration in liver, kidney, heart; fatty, vacuolar changes in hepatic cells of central lobular zone; oedema, hemorrhage in pulmonary alveoli in some. Survivors of percutaneous MLD showed slight degeneration of hepatic cells. 3122 2824

h) Chickens, receiving oral LD$_{50}$: Post mortem: Congestion, oedema of lungs; liver, kidney cellular degeneration.

i) Chickens, subchronic experiences: At 6 and 12 ppm in the diet (7 week experiments) highly excitable during 1st week; slightest disturbance precipitated flightiness, nervous chirping, convulsions; lower doses produced proportionately less excitability and symptoms. 2825

5) Hazards, Residues:

a) Extreme caution, with protective measures—gloves, clothing, masks, etc., is de rigueur for formulation and application workers. Ventilation is essential for mixing plants with respirator wearing a sine qua non. 129

b) Not to be used on food and forage crops nearing harvest. 129

6) Phytotoxicity:

a) At insecticidal concentrations and with judicious choice of diluents, particularly in emulsifiable concentrates, the phytotoxic hazard apparently is not high. 129,2120

b) Corn buds are reported to have shown "burning." 129

7) Toxicity for insects:

a) Promising in effectiveness vs. certain Lepidoptera, Hemiptera, Homoptera, for example, European corn borer, corn earworm, sugar beet webworm, tobacco hornworm, thrips, leaf hoppers, aphids, bark beetles, cutworms. The effect is aldrin-like, neurotoxic and with delayed action. 129

b) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Anopheles quadrimaculatus (larva)	Medium	MLC$_{100}$	1.0 ppm		2020
Anopheles quadrimaculatus (larva)	Medium	ca LC$_{70}$	0.1 ppm		2020
Blabera fusca (adult)	inj	MLD $<$ 7 da.	1.5 μg/g	In acetone-triton solution.	1986
Blabera fusca (adult)	inj	Max Td D 7 da.*	2.7 μg/g*	*Maximum Tolerated Dose; in acetone-triton sol.	1986
Chrysops discalis (adult)	Topical	LD$_{50}$ (est.)	60 μg/fly		2707
Chrysops discalis (adult)	Topical	LD$_{90}$	170 μg/fly		2707
Oncopeltus fasciatus	Topical	LD$_{50}$	5.6 μg/g		2231
Protoparce sexta (5th instar)	Topical	LD$_{50}$	87 μg/larva	Large larvae 5.4 (4.1-7.5)g*.	1306
Protoparce sexta (3,4 instar)	Topical	LD$_{50}$	7.6 μg/larva	Medium larvae 2.5 (1.2-4.0)g**.	1306
Protoparce sexta (2,3 instar)	Topical	LD$_{50}$	3.0 μg/larva	Small larvae 0.9 (0.6-1.1)g ***.	1306
Protoparce sexta (5th instar)	Topical	LD$_{90}$	490 μg/larva	Large larvae*.	1306
Protoparce sexta (3,4 instar)	Topical	LD$_{90}$	29 μg/larva	Medium larvae**.	1306
Protoparce sexta (2,3 instar)	Topical	LD$_{90}$	56 μg/larva	Small larvae***.	1306
Protoparce sexta (5th instar)	or	LD$_{50}$	15.3 μg/larva	Large larvae*.	1306
Protoparce sexta (2,3 instar)	or	LD$_{50}$	1.1 μg/larva	Small larvae***.	1306
Protoparce sexta (5th instar)	or	LD$_{90}$	138 μg/larva	Large larvae*.	1306
Protoparce sexta (2,3 instar)	or	LD$_{90}$	3.1 μg/larva	Small larvae***.	1306

c) Comparative toxicity for insects of isodrin and other insecticides:

(1) Toxicity of isodrin and other cyclodienes for Oncopeltus fasciatus and Musca domestica. 2231

Insecticide	Musca		Oncopeltus
	Topical LD$_{50}$ (μg/g)	Relative Toxicity	Topical LD$_{50}$ (μg/g)
Isodrin	—	0.53	5.6
Chlordane (tech)	4.0	1.0 (standard)	145
α-Chlordane	—	1.7	459
β-Chlordane	—	0.56	47
Aldrin	1.6;1.7	0.4	10.3
Dieldrin	1.1;1.5	0.28	15
Endrin	—	0.41	47

(2) Toxicity of isodrin, other cyclodienes and DDT vs. larvae and pupae of *Aëdes*, principally *Aëdes dorsalis*: 2282

Insecticide	% Mortality 24 Hrs. At 1 ppm Among	
	Larvae	Pupae
Isodrin	100	78.8
Aldrin	100	75
Dieldrin	100	79
Endrin	100	95
DDT	87	6
Control	15.2	2.4

(3) Toxicity and speed of action of isodrin and other compounds vs. *Anasa tristis* (adult): 3376

Insecticide	% Mortality 72 hr. At					Rate of Action At Lowest Topical Dosage Giving 90% Or Better Mortality In 72 Hrs.				
							% Mortality At			
	32µg/g	64µg/g	128µg/g	256µg/g	512µg/g	(µg/g)	12 hrs.	24 hrs.	48 hrs.	72 hrs.
Isodrin	—	—	90	100	100	128	0	10	63.3	90
Parathion	100	100	100	100	100	6	3.3	33.3	76.7	90
Lindane	83.3	100	100	100	100	64	—	80	100	100
Aldrin	—	93.3	100	100	100	64	—	23.3	76.7	93.3
Endrin	—	—	100	100	100	128	6.7	20	80.7	100
EPN®	—	—	100	100	100	128	10	26.7	76.7	100
Heptachlor	—	83.3	90	100	100	128	10	50	80	90
Dieldrin	—	—	70	100	100	256	0	70	96.7	100
Chlordane	—	—	36.7	80	90	—	—	—	—	—
Toxaphene®	—	—	16.7	66.7	82	—	—	—	—	—
DDT	—	—	20	30	76.7	—	—	—	—	—

(4) Toxicity of Isodrin and other cyclodienes, for *Blabera fusca* (adults); applied by injection as acetone-triton solutions: 1986

Insecticide	MLD In < 7 days (µg/g)	Maximum Tolerated Dose 7 days (µg/g)
Isodrin	1.5	2.7
Chlordane	8	14
Heptachlor	1.6	5
Aldrin	1.3	2.6
Dieldrin	1.5	2.6
Endrin	1.3	2.5
Solvent Control	454	1388

(5) Toxicity of Isodrin and other compounds for *Chrysops discalis* (adult); topical application: 2707

Insecticide	LD_{50} (est.) µg/fly	LD_{90} µg/fly
Isodrin	60	170
Lindane	4	35
Endrin	9	80
DDT	20	250
Dieldrin	20	950
Methoxychlor	30	90
Aldrin	40	170
Heptachlor	40	200
EPN®	48	120
Chlordane	60	650
Chlorthion®	65	420
Diazinon	90	360
3-Chloro-4-methylumbelliferone,0,0-diethyl thiophosphate	90	910
Q-137	120	400
Malathion	130	330
Toxaphene®	180	480

(6) Toxicity of Isodrin and other insecticides for Protoparce sexta large (L), medium (M) and small (S) larvae: 1306

Insecticide	Topical (μg/larva)						Oral (μg/larva)			
	LD_{50}			LD_{90}			LD_{50}		LD_{90}	
	L	M	S	L	M	S	L	S	L	S
Isodrin	87	7.6	3	490	29	56	15.3	1.1	138	3.1
Endrin	42	2.9	0.51	219	6.3	6.3	9.9	0.11	49	0.85
Parathion	52	9.9	2.8	183	64	12.3	15.7	—	54	—
Lindane	206	—	—	1235	—	—	209	—	398	—
Malathion	481	61	23.6	1276	553	92	355	—	1621	—
Dieldrin	482	—	—	2559	—	—	—	—	—	—
Aldrin	487	—	—	1359	—	—	—	—	—	—
Heptachlor	1058	—	—	4005	—	—	—	—	—	—
Toxaphene®	1363	32	30	5778	138	112	143	—	6025	—
DDD	2622	376	37	9813	2620	367	878	22.5	2192	58
DDT	≫4000	2334	366	—	9887	1342	4416	158	28040	1125

(7) Toxicity of isodrin and other substances, vs. Sphenarium purpurascens; corn field tests: 307

Insecticide		Active Ingredient/Lbs Per Acre	% Mortality After	
			12 Hrs.	24 Hrs.
Isodrin	0.5% spray	0.43	83.2 (81-92)	91.4 (80-96)
Dieldrin	1% dust	0.35	74.2 (68-80)	98.2 (96-100)
Dieldrin	2.5% dust	.88	89.8 (87-93)	99.8 (99-100)
Aldrin	1% dust	.32	77.8 (69-88)	97.8 (95-100)
Aldrin	2.5% dust	.82	88.6 (83.96)	99.6 (99-100)
BHC	1% dust	.36	86.6 (78-92)	94.2 (90-97)
BHC	2.5% dust	.85	93 (89-98)	97 (93-100)
Parathion	0.5% dust	.16	43.6 (36-51)	69.4 (61-80)
Parathion	1.0% dust	.35	66.8 (59-80)	76 (69-84)
Toxaphene	5.0% dust	1.74	26.8 (18-36)	53 (46-60)
Toxaphene	10.0% dust	3.6	40.4 (36-47)	61.4 (55-69)
Chlordane	2.5% dust	.95	32.0 (27-39)	46.6 (41-54)
Chlordane	5.0% dust	1.8	49.6 (39-62)	63.8 (50-77)
Endrin	0.5% spray	.36	32.8 (24-40)	47.6 (43-59)

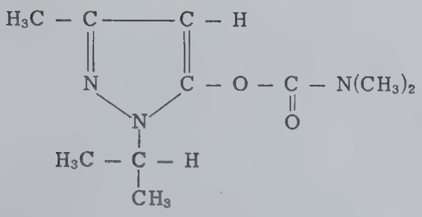
d) Isodrin and beneficial insects:

(1) Isodrin is to be considered potentially hazardous for honeybees. Consult the section in this work titled Bees and Insecticides.

109

1-ISOPROPYL-3-METHYLPYRAZOLYL-(5)-DIMETHYL CARBAMATE

(Isolan; Isopropylmethylpyrazolyl dimethyl carbamate; G-23611.)



Molecular weight: 211.26

GENERAL

[Refs.: 981, 2231, 1285, 1848, 1317, 2942]

A heterocyclic carbamate having a very rapid toxic action for certain insects, and a high order of systemic activity against aphids and other sucking insects, by uptake and translocation in the living treated plant. Isolan is a selective, rather highly specific insecticide in its action on aphids and other sucking forms, since the beneficial predators are reported to be unharmed by either the contact or the systemic action. Not acaricidal in action. Isolan has a high order of stomach, contact, and fumigant toxicity. The systemic action within the plant is producible by soil, foliage, or bark treatment. A related substance, 1-phenyl-3-methylpyrazolyl-(5)-dimethyl carbamate (G-22008, Pyrolan) q.v., is effective vs. houseflies and systemically against Aphis pomi.

Isolan belongs to a group of insecticides which have been referred to as carbamate insecticides or carbamic acid ester insecticides. These substances, related to prostigmine and physostigmine, are characterized by an ability to inhibit powerfully vertebrate and insect choline esterase(s). A general treatment of this group of insecticides may be consulted in this work under the heading Carbamates; Carbamic Acid Esters. Also consult Pyrolan.

PHYSICAL, CHEMICAL

Pure: A colorless liquid; technical: A reddish-brown liquid; b.p. 105°-107°C at 0.5 mm Hg; volatility: 500 mg per 100 g as a vapor at 100°C; miscible with water, alcohol, acetone, xylene.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	12-18	In water solution.	1285
Rat	or	LD_{50}	54	As a 20% emulsion.	1285

a) On the basis of the above LD_{50} values, Isolan may be considered highly toxic.

2) Phytotoxicity:

a) Experimental application to various plants in concentrations sufficient to give effective systemic insecticidal action suggests that, at these levels at least, Isolan is not phytotoxic. Some bark injury to apple trees from petroleum jelly—Isolan applications are believed due to the jelly rather than to Isolan. 1285 981

3) Toxicity for insects:

a) Aphis sambuci (wingless adults) tested on glass plates with Isolan at 0.01 μg/100 cm^2 showed 50% "knock-down" or kill in 35-41 minutes; 100% "KD" or kill in 97-109 minutes. 1285

b) Aphis sambuci (wingless adults) tested on glass plates with Isolan at 0.001 μg/cm^2 showed 50% "KD" or kill in 45-50 minutes; 100% "KD" or kill in 105-110 minutes. 1285

c) Doralis sambuci: LD_{50} ca. 0.015 μg/g; LD_{100} ca. 0.025 μg/g. 1285

d) Aphis rumicis: Spray at 2g/100 l water gave 100% kill in 180 minutes. 1285
Aphis rumicis: Spray at 10g/100 l water gave 100% kill in 45 minutes.

e) Musca domestica, effective concentration as a deposit: 0.01 mg/cm^2. 1317

f) Orchard aphids, in field treatments with sprays at 4-8 g/100 l water, gave kills equal to parathion at dosages 5-6 times greater. 1285

g) Doralis fabae (on Vicia faba): Complete suppression for 7 days by treatment with 0.005-0.01% Isolan sprays; Myzodes persicae suppressed for 3-5 days with sprays at 0.005-0.01% Isolan; at concentration of 0.02% Isolan suppressive action vs. Doralis fabae endured for 15 days; for Myzodes persicae endured 7-13 days. 1285

h) Phylloxera vastatrix with Isolan sprays, at concentration of 0.008%, showed mortalities of 25% at 24 hours, 47% at 72 hrs, 49% at 456 hrs. 1285

i) Effectiveness of Isolan, compared with certain other insecticides, vs. Musca domestica (adult), tested with Contact Sprays by the turntable modification of the Peet-Grady method: 2033

Insecticide	Spray Concentration (mg/cc) To Give 50% Kill In 24 Hrs. (LC$_{50}$ 24 Hr. [approx.])	"Knockdown" In 10 Minutes At LC$_{50}$ (approx.) 24 Hrs.
Isolan	1.15	100%
Dieldrin	.017	0
Parathion	.02	0
Methyl parathion	.025	0
Lindane	.046	0
Heptachlor	.052	0
Aldrin	.056	0
TEPP	.069	ca 70%
Chlordane	.25	0
DDT	.35	0
Malathion	.48	0
Toxaphene®	.68	0
Tetrapropyl dithiopyrophosphate	.69	0
Dilan	.72	ca 30%
Pyrolan	5.5	100%
Allethrin	1.5	100%

j) Effectiveness of Isolan compared with Dimetan and Pyrolan for several insect and one acarine species: 981

Insect or Acarine	Dosage oz/100 gal.	% Mortality With		
		Isolan	Dimetan	Pyrolan
Tetranychus bimaculatus (nymph)	32	6	13	43
Prodenia eridania (1st instar)	32	10	25	35
Macrosiphum pisi (wingless adult)	32	100	100	100
" "	8	100	49	80
" "	2	70	5	6
Epilachna varivestis (1st instar)	32	100	100	—
" "	8	100	85	—
" "	2	95	5	—
	mg^2/ft^2			
Musca domestica (adult)	200	—	100	—
" "	50	100	97	100
" "	10	98	24	81
Periplaneta americana (4th instar)	200	100	100	100
" "	50	100	100	100
" "	10	95	15	85
Mouse or LD$_{50}$ (mg/k)		18	140	90

k) Effectiveness of Isolan compared with lindane vs. Aphis pomi: 981

Insecticide	Dosage Oz/100 gal.	% Mortality 24 Hrs.
Isolan	1	89.5
Isolan	4	98.0
Lindane	4	8.0

4) Action of Isolan on Insects; uses: 1285, 981

a) Insecticidal action is by ingestion (most important), contact, fumigation, or systemic translocation to leaf surface. The action is particularly potent vs. aphids. The mode of action is presumed to be one of insect choline esterase(s) inhibition. The toxic symptoms in insects appear more rapidly with Isolan than with Dimetan or Pyrolan. Among susceptible insects are aphids, psyllids, coccids, acarines, but for all save aphids concentrations must be elevated.

b) The differences of susceptibility between Brevicoryne brassicae and Myzodes persicae, noted with other carbamates, are less marked with Isolan. Action vs. sheltered, leaf-curling aphids, for example Brachycaudis helichrysi or Sapphaphis pyri is strong.

c) Duration of the effectiveness depends on species of aphid, concentration, physical factors, physiology of the treated plant. The effect is most prolonged on mature plants at end of growth period.

d) Systemic action of Isolan:

(1) Systemic uptake and translocation in sap to all parts of treated plant have been demonstrated.

(2) Trees may be treated by painting of the trunk or via the soil. For example, 10% Isolan in petroleum jelly applied in bands to apple tree trunks killed woolly aphids (Eriosoma lanigerum) in 2-5 days after application and kept trees free for from 2 months to season-long. Aphids on birch and black locust were also controlled; aphids on maple were not controlled. Aphids on plums, pears (and cabbage) have been systemically controlled. Promising results were obtained vs. thrips but in no cases have acarines been controlled.

(3) Isolan is active at lower concentrations than Systox® or Pyrazoxon, q.v., vs. Aphis pomi. Penetration to sap is more rapid for Isolan; 100% kills on trees after 3 days as compared to 9 days with Systox® and Pyrazoxon at higher concentrations. Duration of effectiveness was superior to that of Systox® or Pyrazoxon; aphicidal action of 75 days has been obtained. Duration of systemic action was decidedly greater than that of contact action. Trunk painting yielded longer action than foliage treatment. Stability in plant sap is indicated.

(4) Rapid translocation depends on a normal transpiration stream in the plant. On branches of a young appletree, receiving 400 mg at base of trunk, aphicidal action began in 24 hrs. on the branches at a relative humidity of 52-68%, with 100% kill of aphids in 72 hrs; at 90-95% relative humidity feeble aphicidal action was had at 72 hrs; 10 days was necessary for 100% kills. Action was best on healthy trees as compared with those already heavily aphis-damaged for example by Sapphaphis plantaginea. Nature of the bark is likewise a factor.

(5) Treatment of "seed" potatoes produced potato plants aphid-free for ca. 6 weeks; in case of Myzodes persicae (winged form), vector of potato virus diseases, the effect was not sufficiently enduring to forestall infestation.

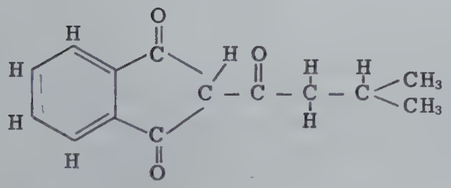
(6) Action against natural insect predators of aphids: Non-sucking insects are not intoxicated by Isolan. Adult coccinellids and chalcids are resistant, but on the larvae of coccinellids, syrphids and chrysopids the action is more violent than that of OMPA (Schradan) probably by feeding on poisoned aphids.

(7) ID_{50} of insect cholinesterases; Isolan: 2659

Choline Esterase Source	ID_{50} (M) (in vitro)
Dacus dorsalis	7.2×10^{-8}
Dacus cucurbitae	8×10^{-8}
Ceratitis capitata	1.2×10^{-7}

110

2-ISOVALERYL-1, 3-INDANDIONE (Valone®; Isovaleryl indandione)



Molecular weight: 210.232

GENERAL

(Also see 2-Pivalyl-1,3-indandione) [Refs.: 1793, 353, 2231, 2120, 129, 1801, 1510, 2024, 919, 2741, 992, 1741, 149, 1832, 2184]

A compound whose insecticidal properties were first reported in 1942. The general class of compounds to which Valone® belongs contains several pesticides useful not only against insects, but also, by virtue of anti-blood-coagulant properties for mammals useful as rodenticides. Valone® is a powerful contact insecticide useful to replace the greater part of the pyrethrins in fly sprays. Valone® is also a potent louse killer and highly effective against chiggers and ticks. Within the general group, the 2-acyl-1,3-indandiones, of which Valone® is one, effectiveness for Musca domestica increases with chain length from acetyl (C_2) to valeryl, isovaleryl, pivalyl (C_5), after which, with increasing chain length or aromatic substitutions, toxicity for Musca declines. Evidence has been presented indicating a possible synergistic action of Valone® with BHC. Valone® and its relatives have a high toxicity for mammals in multiple doses, while having a relatively low single dose toxicity. An interesting property of Valone® and other indanediones, e.g., Pival, is a systemic action on lice after the administration of the substances orally to animals, for instance, rabbits.

PHYSICAL, CHEMICAL

A yellow, crystalline solid; m. p. 67°-68°C; virtually insoluble in water; soluble in most organic solvents; soluble, with formation of bright yellow salts, in aqueous alkalis and ammonia.

TOXICOLOGICAL

1) Toxicity for higher animals: 1741

a) Oral administration in olive oil solution: 1741

Animal	Number	Dosage (mg/k)	% Mortality
Rat	5	100	20
Rat	8	200	100
Rat	6	300	100
Rabbit	4	100	0
Rabbit	3	150	67
Rabbit	3	200	100

b) Minimal daily doses (mg/k), by intraperitoneal injection, yielding at least 50% mortality in 7 days; Rats: 2741

Indandione	Daily Dose (mg/k)	Total (mg/k)	% Mortality	Number Of Subjects
Isovaleryl	10.0	50	67	6
Isovaleryl F^{++}salt	10.0	50	92	12
Isovaleryl Cu^{++}salt	10.0	50	50	6
Isovaleryl Cu^{+}salt	10.0	50	50	6
Pivalyl	5.0	25	67	12
Pivalyl Fe^{++}salt	5.0	25	83	12
Diphenyl acetyl	0.1	0.5	39	18
Diphenyl acetyl Fe^{++}salt	1.0	5.0	100	18
Phenyl acetyl	5.0	25	92	12
Acetyl	10.0	50	50	6
Benzoyl	10.0	50	0	12

c) Mortality, Rats, after single intraperitoneal injections: 2741

Indandione	Dose (mg/k)	% Mortality	Number of Subjects
Diphenyl acetyl	1	0	12
"	5	39	18
"	10	39	18
"	25	67	24
"	50	83	18
Phenylacetyl	5	0	12
"	10	25	12
"	25	50	12
"	50	92	12
Pivalyl	10	0	6
"	25	17	6
"	50	42	12

d) Signs and symptoms in rats intoxicated with Valone® by oral administration in olive oil: 1741

(1) Labored respiration, progressive muscular weakness, hyperexcitability, pulmonary congestion, venous engorgement, systolic standstill of the heart, death in 2-12 hours. As a rule, no hemorrhages observed. Prothrombin time greatly elevated. Vitamin K, as 2-methyl-1,4-naphthoquinone, exercised little if any, effect on Valone® treated rats.

2) Sub-chronic toxicity; administration of Valone® in diet of Rats: 1741

Number of Subjects	% Valone®	% Dead At			
		5-7 days	8-11 days	12-15 days	16-20 days
10	0.1	100	—	—	—
10	0.06	90	10	—	—
5	0.01	100	—	—	—
6	0.01	33	33	33	—
6	0.01 (+.5% Vitamin K)	33	33	33	—
12	0.005	25	33	17	25
12	0.005(+ .2% Vitamin K)	8	17	42	33
6	0.1	100	—	—	—
6	0.05	100	—	—	—

a) Animals continued to gain weight showing no symptoms until just before death. 1741

b) At post mortem: Marked internal haemorrhage, fatty degeneration of liver with focal necrosis, disappearance of plasma prothrombin. 1741

c) Rabbits:

(1) Of 55 rabbits, receiving 4-9 doses, 50 mg/k in olive oil daily for a total of 0.2-0.4 g/k, all died (100% mortality).

(2) Symptoms included: From no symptoms to oral and nasal haemorrhage, haemorrhage after venipuncture. At necropsy: Thoracic and pulmonary haemorrhages, pleural effusion with blood, albuminuria.

3) Pharmacological, pharmacodynamic, physiological, etc.; higher animals: 851, 992,1741

a) Certain indanediones produce anti-coagulant effects similar to those brought about by compounds of the coumarin series.

b) The action is by a decrease of prothrombin formation in the liver leading to a hypoprothrombinemia.

c) When such compounds, for example 2-phenyl-1,3-indandione (which is used clinically), are used therapeutically the first indication of haematuria dictates discontinuance until prothrombin reaches safe blood levels. The activity of 2-pivalyl-1,3-indandione is approximately equal to that of dicoumarol.

4) Toxicity for insects: (1,3-indan(e)dione insecticides)

a) Of principal interest insecticidally are: 2-valeryl-1,3-indan(e)dione, 2-isovaleryl-1,3-indan(e)dione, 2-pivalyl-1,3-indan(e)dione. 1793

(1) Compounds with active methylene between 2 oxo-groups, as the dominant functional group, are toxic to insects.

(2) Toxicity is enhanced by acylation of the active methylene group.

(3) Preparation is by the Claisen condensation between methylketones and phthalic esters. The discovery of the toxicity of Valone® for Musca has led to a long series.

(4) All the acyl derivatives prepared have some insecticidal activity; size and structure of acyl group exercise profound influence on toxicity. As carbon increases from 2-5, effectiveness rapidly increases, but at higher carbon numbers declines as rapidly.

(5) Substitution of bromine for 1 hydrogen of the ring in 2-isovaleryl-1,3-indan(e)dione decreased markedly the insecticidal power, as did methylation of acidic hydrogen.

(6) 2-pivalyl-1,3-indandione is the only member of the series with a higher toxicity for insects than the original 2-isovaleryl-1,3-indandione (Valone®).

b) By the Peet-Grady Test, acylated 1,2-indandiones prove very toxic to Musca domestica. The isomeric valeryl indandiones exert a potent insecticidal action approaching that of the pyrethrins, but the action is not rapid enough for use alone in contact sprays. Useful, therefore, as substitutes for major part of pyrethrins, especially in more concentrated insecticides.

c) Toxicity of 2-isovaleryl-1,3-indandione (Valone®) (in terms of pyrethrins), and other 1,3-indandiones for Musca domestica by the Peet-Grady Test; formulated in deodorized kerosene at 500 mg/100 cc + pyrethrum extract to give 50 mg pyrethrins/100 cc of spray. Any kill in excess of 30% is due to accompanying indandione. Pyrethrins provide rapid paralysis without materially increasing killing power. 1741

Indandione	Readjusted % Kill (Isovaleryl = 80%)	Pyrethrin Equivalent* mg/100cc	% Activity Compared With Pyrethrins	M.P.°C (Uncorrected)	Ketone Used In Claisen Condensation
Acetyl	37	23	5	109-111	Acetone
Propionyl	49	48	10	101	Methyl ethyl ketone
Butyryl	63	80	16	29-30	Methyl propyl ketone
Isobutyl	58	66	13	96	Methyl isopropyl ketone
Isovaleryl (Valone®)	80	140	28	67-68	Methyl isobutyl ketone
Pivalyl	89	210	42	108.5-110.5	Pinacolone
Caproyl	63	80	16	3735-38	Methyl amyl oxide
Enanthoyl	51	52	10	oil	Methyl hexyl oxide
Hexahydrobenzoyl	70	100	20	79-80	Methyl cyclohexyl oxide
Benzoyl	50	50	10	109-110	Acetophenone
β-Naphthoyl	40	30	6	140-142	Methyl-β-naphthyl ketone
Senecioyl	33	13	3	135	Mesityl oxide
No Acyl Group	35	20	4	—	—
50 mg/100 cc Pyrethrins alone	30**	—	—	—	—
Valeryl	—	—	—	oil	Methyl butyl ketone
β-Phenyl propionyl	—	—	—	77	4-Phenyl-2-butanone
α-naphthoyl	—	—	—	193-194	Methyl-α-naphthyl ketone
5-Bromo-2-isovaleryl	—	—	—	122-124	Methyl-isobutyl-ketone

* = The amount of pyrethrins which would have to be added to the 50 mg/100 cc solution to yield the kill obtained by the corresponding acylated indandione + 50 mg/100 cc pyrethrin combination.

** Thus any kill in excess of 30% may be considered due to the accompanying indandione.

5) Pharmacological, pharmacodynamical, physiological, etc.; insects: 2600,2599

a) May be considered a liposoluble, neurotoxic insect toxicant. Effective by contact to Musca, lice, acarines, but almost ineffective by contact, or orally, for Periplaneta americana.

(1) Injected into haemolymph or tracheae of Periplaneta produced rapid effect with complete paralysis in a few minutes with blockage of all nerve transmission and no recovery.

(2) Sub-lethal doses gave no effect.

(3) On tracheal injection showed immediate paralysis which could be localized with no transmission of the effect elsewhere to nerve system.

(4) On topical, oral, administration gave similar effects but these could require days to occur and some individuals are not at all affected.

(5) By whatever route, once there is enough effect for paralysis there is no recovery. The variability is in the time required and whether effect develops at all.

(6) Not an inhibitor of choline esterase.

(7) Neural effects (by any route): Complete loss of birefringence, destruction of ultra-structure responsible for optical properties of axoplasm (optical changes may be followed in excised nerve cords on Valone® application, and they appear in 2-4 minutes or more, at all events in a time interval longer than that required to bring on paralysis in vivo). Optical effects appear subsequently to irreversible paralysis.

The effect on the axis cylinder is drastic and in absence of any demonstrable effect on nerve sheath. Histologically the nerve cord is practically normal; this is true of the axis cylinder in spite of the degeneration of the optical properties of normal tissue. The only histological abnormality notable is chromatin clumping (nuclear pycnosis), which may be as much an effect of acidity as of Valone® injury. The micellar proteins of the neuraxones are profoundly altered, while the lipoidal nerve sheath is unaffected.

6) Other comments:

a) In control of chiggers (Eutrombicula alfreddugesi, Acariscus mansoni, Acarina) 25 lb/acre gave virtually complete control. 2024

b) Vs. adult lice: Equal to the best for fast ''knockdown'' (among other excellences). 919

c) For screening data, indicating superior insecticidal action vs. lice (eggs, adults) fleas, ticks, chiggers, mosquito larvae, Periplaneta americana, mosquito repellency consult Ref. 1801.

111

LAURYL THIOCYANATE (n-Dodecyl thiocyanate; Dodecyl thiocyanate; Lauryl rhodanate; Loro®.)

$CH_3(CH_2)_{11}SCN$ Molecular weight 227.404

GENERAL [Refs.: 353,311,414,2124]

A member of a group of insect toxicants which have been referred to collectively as Lethanes® or organic thiocyanates. A general treatment under the latter title is given in this work and may be consulted for a discussion of common and contrasting properties of these insecticides. Lauryl thiocyanate, as is typical of insecticides of fatty acid derivation, is an effective aphicide. In this respect, it represents the peak of toxicity of a series of n-alkyl thiocyanates whose contact toxicity for the aphids, *Myzus persicae* and *Macrosiphoniella sanborni*, and the red spider mite *Tetranychus bimaculatus*, increases with the lengthening of the carbon atom chain to the point of C_{10} to C_{12} chain length, thereafter decreasing in effectiveness. Strongly ovicidal. Toxicity low for mammals.

PHYSICAL, CHEMICAL

A dark, brown, mobile liquid; b.p. 170°-172°C at 10 mmHg; virtually insoluble in water; soluble in most organic solvents and oils. 311

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	1250	Low toxicity; at lethal levels kills quickly.	1949

- a) Considered non-toxic for man and warmblooded animals. Lauryl thiocyanate, undiluted, kills only when taken in quantities relatively great. 449
- b) Mammalian toxicity increases in descending the alkyl series to methyl thiocyanate, for which the oral LD_{50} (for the rat) is 60 mg/k.
- c) Subcutaneous administration is said to be 300-600 times as toxic as oral administration. 3201
- d) All the higher alkyl thiocyanates are skin irritants; all may be absorbed via the skin in toxic amounts. 1859,3201 1949,414

2) Mode of action in higher animals:

- a) Virtually no data exist for the higher alkyl thiocyanates. They are described as paralytic, but not narcotic, poisons acting on the central nervous system. 3062 1221
- b) Symptoms of poisoning by organic thiocyanates generally comprise restlessness, severe depression, cyanosis, dyspnoea, tonic convulsions with death from respiratory paralysis. Death, after a lethal dose, is swift.
- c) Pathological signs of organic thiocyanate poisoning are: A vacuolation of the hepatic cells, and monocytic fibrinous pneumonitis. 1951 2078

3) Phytotoxicity:

- a) Considered, in general, not to be phytotoxic. 2120

4) Toxicity for insects:

- a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Cimex lectularius (adult)	Contact Spray	LC_{50}	19.5%	Sprayed as white oil sol at a deposit rate of 0.36 mg/cm^2.	413
Pediculus humanus corporis (adult)	Contact Spray	LC_{50}	5.0%	" "	414,636
Pediculus humanus corporis (adult)	Contact Spray	LC_{50}	6.0%	" "	413
Pediculus humanus corporis (adult)	Contact Spray	LC_{50}	0.5%	Sprayed as aqueous preparation at a deposit rate of 1.8 mg/cm^2.	413
Pediculus humanus corporis (eggs)	Contact Spray	LC_{50}	1.0%	" "	413
Pediculus humanus corporis (eggs)	Contact Spray	LC_{50}	18.0%	Sprayed as white oil sol. at a deposit rate of 0.36 mg/cm^2.	414 636
Periplaneta americana (adult ♂♂,♀♀)	inj	LD_0	0.4 mg/g	As a mixture, Lorol thiocyanate, 93%	2219
Periplaneta americana (")	inj	LD_{50}	0.9 mg/g	total thiocyanates of which lauryl	2219
Periplaneta americana (")	inj	LD_{100}	1.5 mg/g	thiocyanate = 60%.	
				Av. wgt ♂ 0.9 (.7-1.15)g	2219
				Av. wgt ♀ 1.3 (1.0-1.9)g	
Aphis*	Contact Spray	LC_{50}	1:3000	*= "Green Chrysanthemum aphid"	311

b) Chemical structure and toxicity; comparative toxicity:

(1) Toxicity and chain length of alkyl thiocyanates: 414,311

Compound	LC$_{50}$* (%) For Pediculus humanus corporis (Contact Spray)	LC$_{50}$ Aphid (Green Chrysanthemum) (Contact Spray)	Carbon Atoms, (No.)
n-Hexyl thiocyanate	—	1:1200	6
n-Octyl thiocyanate	5%	1:2500	8
n-Decyl thiocyanate	5%	1:2800	10
n-Dodecyl thiocyanate (lauryl)	5%, 6%	1:3000	12
n-Tetradecyl thiocyanate (myristyl)	11%	1:2700	14
n-Hexadecyl thiocyanate (cetyl)	18%	1:1700	16
n-Octadecyl thiocyanate (stearyl)	25%	—	18

*Sprayed in white oil at a deposit rate of 0.36 mg of liquid/cm^2.

(2) Toxicity of lauryl thiocyanate and other compounds, for Pediculus humanus corporis (adult). Contact sprays applied in white oil at a deposit rate of 0.36 mg liquid/cm^2: 414 636

Insecticide	LC$_{50}$ (%)	
Lauryl thiocyanate	5.0	
β-Butoxy-β'-thiocyanodiethyl ether	1.5	(Lethane® 384)
Thiocyanoethyl laurate	8.1	(Lethane® 60)
DDT	0.3	
DDD	0.9	
Methoxychlor	0.9	
Lindane	0.02	
DFDT	1.4	
p-Chlorophenyl chloromethyl sulfone	0.1	

(3) Toxicity of lauryl thiocyanate and other compounds for eggs of Pediculus humanus corporis (mixed ages [recently laid eggs are more susceptible than others]) treated with contact sprays in P$_{31}$ white oil, sprayed to give 0.36 mg liquid/cm^2: 413

Insecticide	LC$_{50}$ (%)
Lauryl thiocyanate	18
β-Butoxy-β'-thiocyanodiethyl ether	6
DDT	> 3% (saturated sol) → 8% kill only
Bis-ethyl xanthogen	>50% → 30% kill only
Benzyl benzoate	>50% → 40% kill only
Thanite	>50% → 15% kill only

(4) As aqueous contact sprays (emulsions), at rate of 1.8 mg liquid/cm^2, for eggs of Pediculus humanus corporis; adults: 413

Insecticide	LC$_{50}$ (%) approximate	
	Adults	Eggs
Lauryl thiocyanate	0.5	1.0
Rotenone	0.15	—
Formaldehyde	9.0	25.0
Lysol	12.0	5.0

(5) Toxicity of lauryl thiocyanate and other thiocyanates, for Pediculus humanus corporis and Cimex lectularius (adults); as direct contact sprays in P$_{31}$ white oil, sprayed at rate of 0.36 mg/cm^2: 413

Compound	LC$_{50}$ (%) For		
	P. humanus corporis	C. lectularius	Ratio
Lauryl thiocyanate	6.0	19.5	3.2
Lethane® 384	1.5	4.0	2.7
Lethane® special	2.4	12.5	5.1
Lethane® 60	8.1	32.0	3.9

(6) Toxicity of lauryl thiocyanate and other insecticides, for Pediculus humanus corporis and Cimex lectularius (adults); as direct contact sprays in P$_{31}$ white oil, applied at rate of 0.36 mg liquid/cm^2: 413 414

Insecticide	LC$_{50}$ (%) (30, 40 Insects/test)	
	Pediculus	Cimex
Lauryl thiocyanate	6.0	19.5
Lindane	.016	.051

(6) Toxicity of lauryl thiocyanate and other insecticides, for *Pediculus humanus corporis* and *Cimex* 413
lectularius (adults); as direct contact sprays in P_{31} white oil, applied at rate of 0.36 mg liquid/cm^2: 414

Insecticide	LC$_{50}$ (%) (30, 40 Insects/test)	
	Pediculus	Cimex
Pyrethrins (+ 2% isobutyl undecylenamide)	.038	.026
Pyrethrins	.47	.045
DDT	.03	.56
Lethane® 384	1.5	4.0
Lethane® special	2.4	12.5
Lethane® 60	8.1	32.0
Thanite	3.2	75.0
Bis-ethyl xanthogen	6.2	75.0
Benzyl benzoate	21.0	75.0

(7) Toxicity of lauryl thiocyanate and other compounds for *Pediculus humanus corporis* (eggs, adults) and *Cimex lectularius* adults, as dusts (*per se* or in kaolin). 413

Substance	Concentration (%)	% Mortality		
		Pediculus		Cimex
		adults	eggs	adults
Lauryl thiocyanate	10	100*	100	100
DDT	10	100*	0	100
"	5	100*	—	100
"	1	100	—	96
"	.5	61	—	35
"	.25	12	—	—
Lindane	10	—	0	—
"	.1	100*	—	100
"	.01	100*	—	25
"	.005	90	—	0
"	.001	0	—	—
AL 63	—	100*	100	83
Rotenone in AL 11	1.0	100*	0	75
"	.5	95	—	—
Diphenylamine	100	100*	100	100
"	10	100	56	83
Thiodiphenylamine	100	40	10	0
Dinitroanisole	100	100*	100	33
"	10	50	96	—
Boric acid	100	0	0	5
Sodium fluoride	100	0	0	15
Mercurous chloride	100	0	0	15
Mercuric chloride	100	100	—	100
Sulfur	100	15	0	0

*Complete kill in 24 hours.

(8) Toxicity of lauryl thiocyanate and other compounds, on flannel fabric, for *Pediculus humanus corporis*. 414
Toxicants sprayed on fabric in oil or a volatile solvent:

Insecticide	Approximate LD (Active Principle) mg/cm^2		
	(50% In Oil)	(10% In Oil)	(In Volatile Solvent)
Lauryl thiocyanate	0.06	0.04	0.45
Lethane® 384	—	.02	—
Lethane® special	—	.02	—
Pyrethrins	.006	.0045	.031

(1) All thiocyanates under certain circumstances irritate human skin.
(2) Man, working and sweating freely, experiences severe burning sensation, erythema especially from Lethane® 384, but less so from Lethane® Special or lauryl thiocyanate.
(3) Toxic effect much reduced by washing of treated fabric, although all gave 100% kill after 7-10 days wearing even after 3 months prior storage.
(4) Lauryl thiocyanate gave 100% kill after 11-16 days wearing; at 50% conc. gave 100% kill after 17-22 days wearing; at 85% gave 100% kill after 20-30 days wearing.
(5) Lauryl thiocyanate controls *Phthirius pubis*.

5) Screening tests:
For screening tests against lice, mosquito larvae, adults, flies (adult), cockroaches, fleas, lice, ticks, chiggers and for repellency, consult Ref. 1801.

112

LEAD ARSENATE (Diplumbic hydrogen arsenate; Dilead orthoarsenate; Acid lead arsenate; Gypsine.)

$PbHAsO_4$ Molecular weight 347.13

GENERAL (Also consult in this work the general treatment, Arsenic, Arsenicals)
[Refs.: 986,353,2120,129,2815,1059,757,484]

An insecticide which has long been in general use to control chewing insects and some soil-inhabiting forms. The action of lead arsenate is primarily that of a stomach poison, although it is not devoid of contact action. There is a number of different chemical substances which are known as lead arsenate, but the two commonly used as insecticides are acid lead arsenate (formula above), and basic lead arsenate (lead hydroxyarsenate) $Pb_4(PbOH)(AsO_4)_3$. Either form should contain a minimal amount of arsenic pentoxide to minimize phytotoxic damage. From the phytotoxic point of view, both these salts are less hazardous than calcium arsenate or Paris green, with basic lead arsenate being less hazardous for plants (but also less toxic for insects) than acid lead arsenate, and it is generally acid lead arsenate which is meant when the term lead arsenate is used with reference to insect poisoning. Lead arsenate is toxic to mammals to a high degree, 10-50 mg/k being generally lethal. Lead arsenate has had a long and honorable career as one of the most useful of economic insecticides and only the development of organic synthetics and certain natural plant products has brought about a partial eclipse of this substance. Nonetheless vast quantities are still used, and cost, familiarity with its use and its advantages and disadvantages as well as its excellence, still assign a place for lead arsenate among the weapons for control of major economic insect pests. Do not apply to food crops within 30 days of harvest.

PHYSICAL, CHEMICAL

A heavy white powder (regulations in many states require the addition of a pink coloring matter as a safety measure); decomposes at temperatures higher than 280°C; $d^{15°}_{15°}$ 5.786-5.930 (amorphous form) $d^{15°}_{15°}$ 6.05 (pure, crystalline form); virtually insoluble in water (commercial product: Soluble as arsenic in distilled water; 0.4%; in hard water: 4.4%; pure form soluble in water to 0.002%); no odor; salty taste; stable toward light, air, moisture, and carbon dioxide; not stable toward acids and alkalis.

a) Formulations: Formerly as paste preparations containing not less than 14% arsenic as As_2O_5; at the present time chiefly as a powder of not less than 32% arsenic (as As_2O_5) content, the powders to be made up and applied as suspension sprays, ordinarily at 2 lb per 100 gallons of liquid; also used with summer oil emulsions, spray lime and wettable sulfur. Compatible with some of the chlorinated hydrocarbon insecticides and with nicotine sulfate (Black Leaf 40). Also compatible with Bordeaux mixture. Incompatible with soaps (often employed with nicotine sulfate) which act as powerful arsenic-solubilizers.

TOXICOLOGICAL (Also consult general treatment Arsenic, Arsenicals)

1) Acute toxicity for higher animals:

General

a) A daily intake of 0.06 mg of lead or 0.3 mg of arsenic over a period of months is believed sufficient for chronic poisoning. 2221

b) The danger level as residues on the surface of fruit (not absorbed by fruit itself) = 3.6 ppm as As_2O_3 (1940 standard). 353

c) Accidental ingestion is an ever-present hazard where lead arsenate is carelessly stored or handled. Easily mistaken (unless colored in precaution) for common articles of food and seasoning.

d) Removal of residues from fruits is accomplished by washing in water with wetting agent, wiping or brushing. Unless residues are to be removed by such means, application to food crops should not be made within 30 days of harvest. 129

e) In application and formulation, precautions (e.g. goggles, dust mask) should be employed. Skin and clothing contamination should be guarded against.

f) Lead arsenate readily accumulates and becomes fixed in soil, either as a result of use in specific soil 2201
treatment, or by means of spray residues in the soils of treated orchards, vineyards, etc. 2526

(1) Arsenic (as As_2O_3) content of vegetables grown in soils treated with lead arsenate, or grown on the arsenic-containing soils of orchards treated with lead arsenate: 2201

Vegetable	As_2O_3 Content (ppm) When Grown In Soil Treated With Lead arsenate At 250 lbs/acre	500 lbs/acre	1000 lbs/acre
Lettuce	0.1	0.14	0.16
Egg plant	Trace	Trace	Trace

Vegetables Grown On Arsenic Contaminated Orchard Soils

Vegetable	As_2O_3 (ppm) Spots Of Luxuriant Growth crop	soil	Spots Of Retarded Growth crop	soil
Pepper	Trace	48	Trace	100
Cabbage	0	40	"	

(1) Arsenic (as As_2O_3) content of vegetables grown in soils treated with lead arsenate, or grown on the arsenic containing soils of orchards treated with lead arsenate: 2201

Vegetable	As_2O_3 Content (ppm) When Grown In Soil Treated With Lead arsenate At 250 lbs/acre	500 lbs/acre	1000 lbs/acre
Tomato	Trace	Trace	Trace
Carrot	"	"	"
Broccoli	"	"	"
Beet root	0.11	0.1	0.16.
Beet top	0.11	0.11	0.17
Peppers	Trace	Trace	Trace
Snap bean	0	"	"
Radish top	0.23	0.44	0.8
Radish root	0.035	0.23	0.29

Vegetables Grown On Arsenic Contaminated Orchard Soils

Vegetable	As_2O_3 (ppm) Spots Of Luxuriant Growth crop	soil	Spots Of Retarded Growth crop	soil
Peas (seed)	Trace	40	"	166
Peas (pod)	0.16	40	0.48	166
Peas (vine)	0.66	40	0.3	166
Peas (root)	0.19	40	0.33	166
Potato	0.025	40	0.05	88
Squash	0.030	52	0.045	100
Corn (grain)	0	100	0	108
Cucumber	0.021	56	0.023	100
Tomato	Trace	40	—	—
Tomato	Trace	40	Trace	96
Onion (top)	0.4	52	2.25	233
Onion (bulb)	0.02	52	0.11	233
Snap bean	0.06	44	—	—

g) Hazards reported for some domestic animals grazing or foraging in treated orchards: 2404

(1) Orchard treated at 25 lb Lead arsenate per acre: Chickens: No effect; sheep: Symptoms but recovery on withdrawal; calves: Numerous deaths.

(2) At 8.5 lbs per acre: Chickens, sheep: No effect; calves: Anorexia.

h) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	ca. 825		3196
Rat	or	LD_{50}	ca. 100		1951
Rabbit	or	MLD	100	$\frac{1}{5}$ as toxic as As_2O_3 (20 mg/k = MLD).	1870
Rabbit	or	MLD	200		3196
Dog	or	MLD	500	$\frac{1}{5}$ as toxic as As_2O_3 (85 mg/k = MLD).	1870
Sheep	or	LD	4940	As lead monoarsenate.	2162
Sheep	or	MTD*	100	* = Minimum Toxic Dose.	2800
"Mammals"	or	LD	10-50		129,2120
Man	or	LD	100-500		129
Chicken	or	LD_{50}	ca. 450		3196
Rabbit	or	LD_{50}	125		3196
Minnows	Medium	Tolerated	17.1 ppm	1 hr. exposure; in tap water.	2751
Trout	Medium	LC	25 ppm	Death within 24 hrs.	211

2) Chronic toxicity; higher animals:

a) Rats: 4 mg/k/day for 8 weeks gave definite toxic signs; doses less than 4 mg gave growth stimulation, nerve degeneration. 2911

b) Chickens: Reportedly tolerated 830 mg/day for 2 months. 3080,3079

(1) At 1.3-56.7 g/day 18 of 31 birds died; survivors symptomless.

(2) 10 birds taking water with 4800 ppm symptomless at end of 60 days.

c) Cow: Receiving 6.4 g/day (unspecified period) showed no toxic effects. 467

d) Man: 2 individuals, receiving 100 mg over 10 days showed no apparent signs. 2400

e) Daily intake of arsenic 0.3 mg, lead 0.06 mg believed sufficient, over a period of months, for chronic poisoning.

3) Pharmacological, pharmacodynamic, physiological, etc.; higher animals: 851,1221

a) Arsenic of lead arsenate is in pentavalent form; pentavalent arsenic is somewhat less toxic than trivalent arsenic.

(1) The toxicity of pentavalent arsenic in vivo is believed to depend on its reduction to $As^{\equiv}$.

(2) $As^{\equiv}$ powerfully inhibits intracellular sulfhydryl (SH) containing enzymes of cellular respiration. Constitutes the basic mechanism of toxicity.

(3) Arsenicals are fundamental protoplasmic poisons. In man 100 mg of inorganic trivalent arsenicals usually bring severe poisoning.

b) Absorption is easy via all mucous membranes; some dermal intake is possible. Physical state (for instance coarse vs. fine powders) determines the amount of ingested arsenical which is absorbed. Coarse powders are less easily absorbed.

c) Deposition and accumulation in tissues:

(1) Principally, arsenic is accumulated in kidney, liver, intestinal wall; also in lung, skin, spleen, and in lesser amount in brain, muscle. Long exposure brings accumulation in bones and hair.

d) Elimination from body:

(1) Slow, chiefly via urine, feces. Excretion continues long after cessation of intake.

e) In arsenic intoxication the capillaries are dilated and permeability increased; blood pressure falls to shock level.

f) Gastro-intestinal damage, particularly, is severe, a fundamental cause being the severe capillary damage which leads to distention, oedema and fluid engorgement of tissue, blistering, mucosal and epithelial sloughing, diarrhoea, increased peristalsis, etc. Symptoms are cholera-like.

g) Kidneys are affected; nephritis follows capillary damage and direct poisoning of renal tubule cells. Tubular necrosis and glomerular damage are marked.

h) A carcinogenic hazard accompanies chronic arsenosis.

4) Phytotoxicity:

a) Phytotoxic hazard varies with environmental conditions and plant susceptibility. 1079,882,1463

(1) High humidity or slow drying conditions enhance phytotoxic hazard, although lead arsenate, in general, is not deemed highly phytotoxic; damage to foliage, fruit, twig, branch and root is possible.

b) Peach trees are very susceptible; defoliation may be total and twigs killed. 2557

c) Pome species, plum trees: May be damaged at 80°F or more, and in high humidity. 97

d) If bark is intact tree branches and trunk are in little hazard; bark wounds, lenticels and buds may introduce toxic amounts to branch and trunk. 3030

e) Although roots are susceptible, arsenic tends to remain in surface soil above the roots, for instance grapefruit trees showed no injury with 30 lb lead arsenate around base (3000 ppm in soil). Apple trees survived 60 grams of lead arsenate. 3030 2269

f) At 3000 lbs per acre growth of bell peppers was completely halted; 48 lbs per acre depressed growth and yield of cotton, being particularly toxic to roots. 2795 618

g) Lead arsenate in soil; effect on plants:

Plant	% Reduction (At 2000 Lbs/Acre) Of	
	Germination	Growth
Onion	Very slight	Very slight
Tomato		
Pea	Very slight	10-19
Cauliflower		
Brussels sprout		
Squash		
Parsnip		
Cabbage	Very slight	11-37
Lettuce		
Radish		
Turnip		
Corn		
Carrot	Very slight	25-37
Cucumber		
Broccoli		
Okra		
Spinach	13-22	Very slight
Beet	13-22	11-37
String bean	40	25-37
Lima bean	98	—

h) Important to phytotoxicity of lead arsenate is any factor which increases the amount of soluble arsenic; for example alkaline media are powerful solubilizers of arsenic in acid lead arsenate yielding lead hydroxyarsenate + arsenic acid (H_3AsO_4) which yields soluble arsenic. Surprisingly, a temporary safety is conferred by lime—by formation of calcium arsenate which, however, in its turn, with atmospheric CO_2, as H_2CO_3, gives soluble arsenic. 353

i) On sensitive and susceptible plants, for example peach trees, in maritime areas where rain contains NaCl from wind-borne sea-spray, basic lead arsenate is employed, being less soluble and less subject to solubilization. It contains less arsenic than the acid salt, although it is convertible to acid lead arsenate in water at pH 6.5.

j) Comparative phytotoxicity of various arsenicals and lead arsenate for cotton plant seedlings; solutions applied in nutrient solution: 894

Arsenical	% Seedlings Damaged Beyond Recovery At				
	10,000 ppm	1000 ppm	100 ppm	10 ppm	1 ppm
Lead arsenate	100	100	33.3	0	0
Tricalcium arsenate	53.85	76.9	9.1	7.7	0
Copper aceto-arsenite	100	100	100	38.5	9.1
Arsenomethane As-1,2-sulfide	100	70	12	10	0
Chloroarsenomethane As-1,2-sulfide	100	100	100	0	0
DDT	0	0	0	0	0

5) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Alabama argillacea (larva) 5th Instar	or	LD$_{50}$	0.02 (.01-.03) mg/g		1103
Anticarsia gemmatilis (larva)	or	LD$_{50}$	0.12 (.06-.2) mg/g		944
Apis mellifera (adult)	or	LD$_{50}$	5.0 µg/bee	As arsenic element.	231
Bombyx mori (larva, full grown)	or	MLD	27.3 µg/larva	As arsenic element.	586
Bombyx mori (4th instar)	or	LD$_{50}$	0.09 (.057-.121)*mg/g		1381
Bombyx mori (5th ")	or	LD$_{50}$	0.09 (.074-.133)*mg/g		1381
Bombyx mori (4th ")	or	LD$_{50}$	0.09 mg/g		459
Bombyx mori (")	or	LD$_{50}$	0.093 mg/g		387
Bombyx mori (")	or	LD$_{50}$	0.086 mg/g		387
Bombyx mori (")	or	LD$_{50}$	0.062 mg/g		387
Bombyx mori (")	or	LD$_{50}$	0.074 mg/g		387
Bombyx mori (")	or	LD$_{50}$	0.9**		459
Ceratomia catalpae (larva)	or	LD$_{50}$	0.62 mg/g		387
Cirphis unipuncta (larva)	or	LD$_{50}$	0.25 (.20-.34)* mg/g		1381
Cirphis unipuncta (")	or	LD$_{50}$	0.26 mg/g		1742
Datana integerrima (larva)	or	LD$_{50}$	< 0.05 mg/g		387
Datana ministra (larva)	or	LD$_{50}$	0.05 (.02-.1)* mg/g		1381
Datana perspicua (")	or	LD$_{50}$	0.07 (.05-.1)* mg/g		1381
Diataraxia oleracea (larva, last instar)	or	LD$_{50}$	0.066-0.091 mg/larva	Dosage varies with body wgt.	3245
Heliothis obsoleta (larva)	or	LD$_{50}$	0.17 (.11-.29)* mg/g		1381
Heliothis obsoleta (")	or	LD$_{50}$	0.26 mg/g		1742
Hyphantria cunea (")	or	LD$_{50}$	> 0.16 mg/g		387
Malacosoma americanum (larva)	or	LD$_{50}$	0.015-.21		387
Melanoplus differentialis	or	MLD	1.6-3.8 mg/g	Death in 70-156 hrs.	2617
Melanoplus differentialis	or	LD$_{50}$	2-4 mg/g		2617
Melanoplus differentialis	or	LD$_{100}$	4.6-7.7 mg/g	Death in 49-110 (av. 77) hrs.	2617
Periplaneta americana ♂	Topical	LD$_{0}$	0.2 mg/g	Colloidal acid Pb arsenate Insect wgt = .9(.7-1.15)g^{+}.	2219
Periplaneta americana ♀	Topical	LD$_{0}$	0.4 mg/g	" Insect wgt = 1.3(1.0-1.9)g^{++}.	2219
Periplaneta americana ♂	Topical	LD$_{50}$	0.5 mg/g	" +	2219
Periplaneta americana ♀	Topical	LD$_{50}$	1.2 mg/g	" ++	2219
Periplaneta americana ♂	Topical	LD$_{100}$	1.3 mg/g	" +	2219
Periplaneta americana ♀	Topical	LD$_{100}$	2.1 mg/g	" ++	2219
Periplaneta americana ♂	or	LD$_{0}$	0.05 mg/g	" +	2219
Periplaneta americana ♀	or	LD$_{0}$	0.15 mg/g	" ++	2219
Periplaneta americana ♂	or	LD$_{50}$	0.15 mg/g	" +	2219
Periplaneta americana ♀	or	LD$_{50}$	0.4 mg/g	" ++	2219
Periplaneta americana ♂	or	LD$_{100}$	0.6 mg/g	" +	2219
Periplaneta americana ♀	or	LD$_{100}$	1.0 mg/g	" ++	2219
Periplaneta americana ♂	inj	LD$_{0}$	0.2 mg/g	" +	2219
Periplaneta americana ♀	inj	LD$_{0}$	0.3 mg/g	" ++	2219
Periplaneta americana ♂	inj	LD$_{50}$	0.3 mg/g	" +	2219
Periplaneta americana ♀	inj	LD$_{50}$	0.75 mg/g	" ++	2219
Periplaneta americana ♂	inj	LD$_{100}$	0.75 mg/g	" +	2219
Periplaneta americana ♀	inj	LD$_{100}$	1.4 mg/g	" ++	2219
Pieris rapae (larva)	or	LD$_{50}$	0.09 (.09-.10)* mg/g		1381
Pieris rapae (")	or	LD$_{50}$	0.09 mg/g		1742
Pieris rapae (5th instar)	or	LD$_{50}$	0.1 (.07-.14) mg/g		944
Pieris rapae (")	or	LD$_{50}$	0.09 (.07-.12) mg/g		944
Plutella maculipennis (larva)	or	LD$_{50}$	0.041 mg/larva		3244
Polygonia interrogationis (larva)	or	LD$_{50}$	0.06 mg/g (.036-.071)*		1381
Prodenia eridania (larva)	or	LD$_{50}$	0.29 mg/g	Leaf sandwich method; large larvae, 0.7g.	3017
Vanessa cardui (larva)	or	LD$_{50}$	0.16 (.14-19)* mg/g		1381

*=Lowest lethal to highest non-lethal dose.
+ calcium caseinate
+ calcium hydroxide
**Basic lead arsenate.

b) Comparative toxicity, lead arsenate and other compounds for insects:

(1) Vs. Prodenia eridania (larvae 0.7 g body wgt), administered orally by the leaf sandwich method: 3017

Insecticide	LD$_{50}$ (mg/g)
Lead arsenate	0.29
Lindane	0.031
Chlordane	0.13
DDT	0.031

(2) Lead arsenate and other compounds, vs. Diataraxia oleracea (last instar larvae) at various body weights. Administered orally by feeding leaves sprayed by the settling tower method. Pb arsenate as water solution, others as acetone solutions. 3245

Insecticide	Wgt Of Larvae, Grams			Ratio LD$_{50}$: Wgt
	0.32	0.42	0.56	
	LD$_{50}$ µg/larva			
Lead arsenate	66	78	91	1:1.5
TEPP	43	69	112	1:3.3
Parathion	2.6	3.4	4.6	1:2.0
Lindane	13	26	59	1:6.5
DDT	4.5	12	33	1:11.2
Zinc fluoarsenate	Not toxic even at 0.37 mg/larva			
Rotenone	Not lethal even at 0.2 mg/larva			
Pyrethrins	Violently repellent.			

(3) Toxicity for Periplaneta americana of lead arsenate and sodium arsenate compared: (♂ .9 (.7-1.15) ♀ 1.3 (1.0-1.9) grams body wgt.) 2219

(3) Toxicity for Periplaneta americana of lead arsenate and sodium arsenate compared: (♂ .9 (.7-1.15) ♀ 1.3 (1.0-1.9) grams body wgt.) 2219

Insecticide	Route	LD_0 (mg/g)		LD_{50} (mg/g)		LD_{100} (mg/g)	
		♂	♀	♂	♀	♂	♀
Sodium arsenate ($Na_2HAsO_4 \cdot 7H_2O$)	Topical	.03	.15	.10	.5	.3	1.3
Lead arsenate	"	.2	.4	.5	1.2	1.3	2.1
Sodium arsenate	Oral	.08	.6	.25	2.0	.6	6.0
Lead arsenate	"	.05	.15	.15	.4	.6	1.0
Sodium arsenate	Injection	.023	.035	.030	.050	.045	.070
Lead arsenate	"	.2	.3	.3	.75	.75	1.4

(4) Toxicity for Apis mellifera; lead arsenate and other compounds; oral administration: 231,1852

Arsenical	Oral LD_{50} (μg/insect)
Acid lead arsenate*	5.0
Sodium arsenate	1.8
Calcium arsenate	0.7

*Coarse particles (18-28 μμ) much less toxic than fine particles (2-3 μμ); 28 μμ lead arsenate particle size shows LD_{50} values as high as 185 μg/bee.

(5) Control of Pieris rapae and Trichoplusia ni, with lead arsenate and other compounds: Field tests using dust preparations: 796

Insecticide	Concentration (%)	% Control
Lead arsenate	20	77.6
Zinc fluoroarsenate	20	26
DDT	2	87.5
"	3	88.9
Lindane	0.38	84.2
Rotenone	0.75	85.8
Ryania	30	83.1
Sabadilla seed	10	84.5
Pyrethrum	20	78.6
2-Mercapto-6-nitrobenzothiazole	10	3.8

c) Variability in toxicity values of acid lead arsenate vs. Phlogophera meticulosa (5th instar larva) and Plutella maculipennis (last instar larva); Oral administration: 3244

(1) LD_{50} values for P. meticulosa at various larval weights.

Date	Larval Weight (g)		
	0.26	0.43	0.71
	(LD_{50} mg/larva And 5% Level Fiducial Limits)		
October 9	0.047 (.042-.052)	0.074 (.070-.077)	0.117 (.112-.122)
October 11	0.039 (.036-.042)	0.068 (.065-.071)	0.117 (.110-.125)

(2) LD_{50} values at various times of determination for P. maculipennis:

Date	LD_{50} mg/larva
April 10	0.0353 (0.0343-0.0362)
"	.0335 (.0326- .0345)
August 19	.0325 (.0317- .0333)
September 30	.0270 (.0265- .0276)
October 2	.0273 (.0265- .0281)

(3)

LD_{10} (mg/larva)	LD_{90} (mg/larva)
0.0210 (0.0202-0.0219)	0.0348 (0.0339-0.0358)
0.0197 (0.0186-0.0209)	0.0377 (0.0356-0.0401)

(4) Using two methods of presenting data:

Method	LD_{50} (mg/larva)	
	Lead arsenate	DDT
I	0.0340 (0.0316-0.0366)	0.0410 (0.0393-0.0424)
II	0.0330 (0.0315-0.0345)	0.0386 (0.0370-0.0403)

d) Lead arsenate and beneficial insects: [Refs.: 550,573,317,626,850,1228,1578,2038,3346,2650]

(1) Extremely toxic to honeybees: Bees caged on treated blooming apple trees: On sprayed trees 69% mortality; on dusted trees 49% mortality; on untreated trees 19% mortality; death within 3 hours of gathering nectar or pollen from open flowers on treated trees. 2541

(2) Effect of lead arsenate use in apple orchards on parasites and predators of Carpocapsa pomonella: 1688

Condition	Untreated Orchards	Treated Orchards
% eggs parasitized by Trichogramma minutum:	13.9%	5.7%
% larvae, pupae parasitized by Ascogaster:	4.5%	1.4%
% eggs eaten by Leptothrips mali:	12.1%	8.2%
Soil predators: Harpalus, Calathus:	(no.) 2060 (sampling)	(no.) 1687 (sampling)
Ant colonies: Aphaenogaster and Solenopsis:	1096	624
% sound fruit (harvest + drop)	34.6%	67.0%

(3) Spray at 1.5 lbs per 50 gallons exerted no harmful influence on eggs or 1st instar larvae of Hippodamia convergens (aphid predator). 1450

e) Effectiveness as a soil insecticide vs. Popillia japonica: 1026,1939

(1) Most dependable arsenical. (Zinc, ferric arsenates ca. equal to in effectiveness. Basic lead arsenate of no value.)

(2) Aluminum arsenate, dicalcium arsenate, tricalcium arsenate, manganese arsenate, arsenic trioxide gave highly variable results.

(3) Ferric arsenate was less effective, other arsenicals more effective than acid lead arsenate when freshly applied to soil. No correlation noted between water soluble arsenic or arsenious oxide content and effectiveness.

(4) Acid lead arsenate retained effectiveness longer than others in the soil.

f) Pharmacological, pharmacodynamic, physiological, etc.; insects:

(1) Classed for insects as a general protoplasmic poison. The action is primarily that of a stomach poison 353
with some contact potency. 1973

(2) The Pb radical is of secondary importance, but may modify efficacy, for example the metallic arse- 2484
nates in order of toxicity for insects: $Pb > Cu > Ca > Mg > Zn > Fe$. Toxic action of lead arsenate is 3107
attributed to As solely; in Bombyx mori the Pb is all excreted in 24 hours; on Leptinotarsa Pb has 460
little effect. 997

(3) Prodenia eridania, having ingested a toxic amount of lead arsenate: Stopped eating, regurgitated, became inactive and died without convulsion. 3 hours after oral poisoning the midgut epithelium was disintegrating. 3349

(4) Periplaneta americana poisoned by injection: Decrease in activity, then loss of equilibrium followed by loss of recovery (righting) reflexes, succeeded by general asthenia, then weak response to stimulus; finally, no response to stimulus and death. 2327

(5) Analysis of Bombyx mori larvae each of which had consumed 0.0273 mg (as arsenic element) per larva revealed: 0.0027 mg (as arsenic element) per larva in the tissues. 90% of the arsenic taken was voided in the feces before death. Silkworms, receiving a maximum dose of acid lead arsenate, voided in feces only 19% of the arsenic eaten before death. Ceratomia, receiving an average dose, voided 64% of ingested arsenic in feces. 586

g) Resistance to lead arsenate: [1603,1601,1602,1607,2562,3254]

(1) The appearance of resistance, as a result of selection by exposure, in "populations" of Carpocapsa pomonella has been claimed.

(2) Resistant strains of Anarsia lineatella have been observed; 20% of the larvae of these strains penetrated a 0.4% lead arsenate cover on peach twigs as compared with 3% in case of ordinary biotypes. 3012

h) Some reports of field experiences with lead arsenate in economic control of insects:

(1) Pieris rapae: 25% dusts, 0.4% sprays effective in control of. 2226
(2) Protoparce spp.: Controlled by pure dusts, 0.8% sprays. 36,37
(3) Lymantria dispar: 1% suspensions effective against. 353
(4) Prodenia litura: Controlled by. 1264
(5) Cotton Bollworm: Less effective against than DDT. 91
(6) Choristoneura fumiferana: Fair control of with 0.3% sprays; DDT superior. 350
(7) Argyrotaenia velutinana: Controlled by 0.3% sprays. 1199
(8) Polychrosis viteana: Inadequate control by 0.4% sprays. 518
(9) Grapholitha funebrana: Inferior to DDT or parathion, in control of. 578
(10) Carpocapsa pomonella: Best of the inorganic insecticides for control of. 1770,1608,1362,518,2115,2372,440
726,1586,2969,322
(11) Evergestis rimosalis: Effective control, but DDT is superior. 2226
(12) Diaphania hyalinata: " , " . 2226
(13) Alsophila pometaria: Controlled by 0.3% suspensions; DDT superior. 2226
(14) Plutella maculipennis } DDT superior. 2226
(15) Clysia ambiguella } 2226
(16) Melittia satyriniformis: Effective against to some extent; DDT superior. 2226
(17) Thyridopteryx ephemeraeformis: 0.6% sprays gave 100% control; superior to DDT. 2960
(18) Liriomyza orbona: Gave inadequate control of. 1913
(19) Popillia japonica: DDT and others replacing 0.6% sprays of. 343
(20) Macrodactylus subspinosus: Inferior to DDT. 2705

(21) Leptinotarsa decemlineata: 0.6% suspensions control; DDT and others are replacing. 353
(22) Criocoris spp.: Inferior to DDT in control of. 2705,2226
(23) Epitrix hirtipennis: Ineffective against. 353
(24) Anthonomus signatus: Replaced by lindane. 543
(25) Curculio caryae: Inferior to parathion. 2382
(26) Termites: Effective against Reticulitermes flavipes. 1855

113

LIME-SULFUR (Lime-Sulphur; Eau Grison.)

GENERAL [Refs.: 2456,353,129,2120,2749,2750,484]

A complex in long use as a fungicide and as an insecticide against scale insects, aphid eggs, acarine parasites of livestock, etc. Frequently used in association with lead arsenate in orchard protection.

PHYSICAL, CHEMICAL

A deep orange, unpleasant smelling liquid, the commercial standard strength equal to 32° Baumé at 60°F or a specific gravity of not less than 1.283, sulfur content 25% or 2.6 lbs per gallon, with calcium polysulfides being not less than 29% of the total sulfur; the solution (commercial) may be freely diluted with water; essentially a mixture of calcium polysulfides (the active ingredient), ranging from CaS to CaS_5 or higher, with the biological activity increasing with S content and calcium thiosulfate; reaction of solution is somewhat alkaline due to hydrolysis; hydrolyzes readily, particularly upon dilution and exposure to CO_2; of limited compatibility with other materials; decomposed by acids and contact with metallic salts whose metal ions form insoluble sulfides; Liquid lime-sulfur is formed by reactions between calcium hydroxide and elemental sulfur boiled together in water. Theoretically, 3 moles of hydrated lime ($Ca(OH)_2$) and 12 moles S $\rightarrow$ 2 moles CaS_5, 1 mole CaS_2O_3 and 3 moles water. Dry lime-sulfur is made by adding a stabilizer, such as cane sugar, to liquid lime-sulfur and evaporating to dryness; self-boiled lime-sulfur is prepared by taking advantage of the heat of hydration (solution) of CaO to promote the reaction with S.

TOXICOLOGICAL

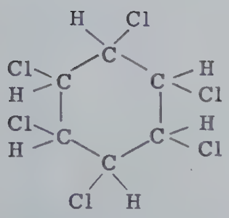
1) Toxicity for higher animals:
  a) No quantitative data available. Applied externally to live-stock, lime-sulfur may cause irritation and general discomfort, even very severe burning of the skin. Rarely does it kill. 2571

2) Phytotoxicity:
  a) Evolved H_2S is responsible for the phytotoxicity associated under certain conditions with lime-sulfur. 2125
    (1) Scorching of the tips and margins of the leaves, with necrotic patches on leaves both young and old may be noted along with premature leaf and fruit fall.
    (2) Pear trees, under drying conditions, may be severely harmed. 2494
    (3) Under high temperature conditions apple trees may be injured severely. The hazard arises at temperatures higher than 26.5°C. 1241
    (4) When used with summer oils severe leaf injury may follow. 1868

3) Toxicity for insects:
  a) No quantitative data available.
  b) On the chorion of Aphis eggs the action is hardening and the contained embryo dries up. 2490
  c) From applications of lime-sulfur, H_2S evolution may continue for 6 hours, but this is insufficient to account for mortality of Aspidiotus. Spontaneous oxidation of lime-sulfur may occur at a rate sufficient to prevent oxygen from reaching the treated scale insects with death ensuing in ca. 18 hours. 2406
  d) Resistance by certain biotypes of San José scale, Aspidiotus perniciosus, developing in response to selection as a result of exposure has long been signalized. 2213 2525
  e) Deemed preferrable to DDT in control of Aonidiella citrina. 353
  f) In some regions Aspidiotus perniciosus is still controlled by lime-sulfur. 353
  g) The larvae of Coleophora laricella may be controlled by lime-sulfur while overwintering. 1501
  h) Lime-sulfur gave 66% control of Tetranychus telarius. 2843
  i) Has been employed in control of Psoroptes bovis on livestock. 2226

114

LINDANE (γ-1, 2, 3, 4, 5, 6-Hexachlorocyclohexane; γ-BHC; γ-Benzene hexachloride; Gamma-isomer of Benzene hexachloride; Gamma-isomer of Hexachlorocyclohexane; 666; Gammexane; Benzahex; Chem Hex; Gamoxo; Gamtox; Hexadow; Isotex; Hexone)



Molecular weight 290.85

GENERAL

(Also consult Benzene hexachloride in this work.)
[Refs.: 1298,2119,1996,2453,1076,2650,1597,1755,3174,873,353,2231,3199,89,2848,2849,1349,1751,2119,2579,2638,1853,171,19,644,2058,1299,642,1824,2924,2822]

Lindane is the accepted common name for the essentially pure gamma-isomer of benzene hexachloride. The gamma-isomer is the principal insecticidal component among the several stereo-isomers of benzene hexachloride, of which there are at least five. As an insecticide of exceptional effectiveness and range, lindane has become one of the most important of contemporary insect toxicants. Since a large amount of comparative data for the various stereo-isomers is given under benzene hexachloride, which will not be repeated here, consultation of the section on benzene hexachloride will be valuable. Lindane is insecticidal by contact, ingestion, and by the fumigant action of its vapors.

PHYSICAL, CHEMICAL

In pure form a colorless crystalline solid with crystals of monoclinic form; m.p. 112.5°C; v.p. mmHg at 20°C = .03, at 40°C = .14, at 60°C = .48; vapor saturation value in air at 25°C = 1.15 μg/l, at 30°C = 1.8 μg/l; virtually insoluble in water (to 10 ppm at 20°C); soluble to a greater or lesser degree in a large number of organic solvents (consult a tabulation given under benzene hexachloride for solubility of lindane in ca. 40 organic substances) as g/100 cc solvent: Acetone 43.5, absolute ethanol 6.7, benzene 28.9, deobase oil 2; in kerosene 3%, in heavy naphtha (b.p. 230-270°) 18%, in paraffin oil (b.p. 138-212°C) 3.2%, ether (g/100 cc) 20.8, xylene (g/100 cc) 24.7; to be known as lindane a product must contain 99% of the γ-isomer and melt at not less than 112°C; odor: None; stable toward air, light, heat, CO_2, strong acids; unstable toward alkalis (by which it is dechlorinated to trichlorobenzenes); incompatible with 10% lime-sulfur solutions, lime, calcium arsenate, various other alkalines; less corrosive than commercial benzene hexachloride.

a) Formulated as dusts; wettable powders; emulsifiable concentrates; in pomades such as vanishing cream; in forms suitable for use in vaporizers or electric light fixtures.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) In acute oral dosage for laboratory animals (rat) lindane, the γ-isomer, is more toxic than any other of the BHC isomers. 1949
   b) The dangerous acute dose for man has been reported as 7-15 g, although severe illness with convulsions has attended a single measured dose of 45 mg (in a young adult) as a vermifuge. 581,89 1882,1240 1239,1589,1823
   c) Lindane is markedly different in toxicity to various species of animals; for laboratory animals it compares favorably with DDT for others, for instance young cattle, lindane is more toxic than dieldrin or DDT. 89
   d) Lindane, volatilized from heat vaporizers, has induced some clear-cut cases of acute human intoxication with great irritation of nose, eyes, throat, nausea and severe headache; overheated lindane is, in particular, acutely irritating.
   e) Since it is absorbable via any route including the skin, precautions are obviously de rigueur.
   f) For higher animals (as an average for all tested) the LD_{50} is given as 125 mg/k (acute oral), the cutaneous danger level as 50 mg/k and the minimum dosage in parts per million to induce chronic toxicity as 400. 1949

g) The maximum vapor concentration for safe exposure of workmen 8 hrs per day is 0.5 μg/l air which is 10 times the recommended lindane concentration for vapor space treatment. High contamination of food products is possible during lindane application by fumigation. Vapors from residual deposits (emulsions or brush applied oil solutions) contaminated packaged or unpackaged food after application to surfaces. Limit of lindane content of stored food (United Kingdom) = 0.5 ppm. 2829 1105

h) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	86		3362
Mouse	ct	LD_{50}	300		451
Rat	or	LD_{50}	177		805,3362
Rat	or	LD_{50}	200		451
Rat	or	LD_{50}	125		1951
Rat	or	LD_{50}	190		3199
Rat	or	LD_{50}	150		596
Rat	or	LD_{50}	230		1823
Rat	sc	LD_{50}	50	Given in peanut oil.	451
Rat	ip	MLD	50		1967,1968
Rat	ip	LD_{50}	35-85	Dosage depends on the solvent used.	596
Rat	ct	LD_{50}	500		451
Guinea Pig	or	LD_{50}	100		451
Guinea Pig	or	LD_{50}	127		3362
Guinea Pig	ct	LD_{50}	400		451
Guinea Pig	sc	LD_{50}	100		451
Rabbit	or	LD_{50}	200	Given in peanut oil.	451
Rabbit	or	LD_{50}	60		3362
Rabbit	ct	LD_{50}	300		451
Rabbit	ct	LD_{50}	>4000	As a dry powder.	1952
Rabbit	ct	LD_{50}	> 180	As a solution.	1952
Rabbit	sc	LD_{50}	75	Given in peanut oil.	451
Rabbit	iv	LD_{100}	4.5-6.0		596
Dog	or	LD	40	Given in oil.	183
Dog	or	LD	100-200		1967
Dog	iv	LD	7.5		183
Calf	or	MTD	5	Minimum toxic dose; single dose.	2567
Cattle	or	MTD	25	" "	2567
Sheep	or	MTD	15	" "	2567
Sparrow	or	LD	100		183
Sparrow	im	LD	26		183
Fish	Medium	Toxic	0.05 ppm		603,2026
Trout	Medium	LC	1-10 ppm		1192
Goldfish	Medium	MTdL*	0.09 ppm	*Median Tolerated Limit; 10 day exposure.	828
Goldfish	Medium	Turnover	25 ppm	Dust 3% γ-isomer, 5% others, 5% DDT.	828

i) Comparative toxicity of lindane and others to Bobwhite Quail and Mourning Dove; oral administration in gelatin capsules: 679

Compound	Quail				Dove			
	LD_{50} (mg/k)	MLD (mg/k)	Average Wgt. Loss (%)	Average Days Lived	LD_{50} (mg/k)	MLD (mg/k)	Average Wgt. Loss (%)	Average Days Lived
Lindane	(♂) 120-130	120	25	3	350-400	200	10	2.5
Lindane	(♀) 190-210							
Aldrin	4-4.5	4	15	3	15-17	12.5	18	4.5
Dieldrin	12-14	10	20	4	44-46	40	15	3
Toxaphene	80-100	40	25	3	ca. 200-250	100	22	3

2) Subacute, sub-chronic, chronic toxicity; higher animals:

a) Cattle:

(1) 3, each sprayed once with 50% lindane (wettable powder): All died. 407

(2) 11 (calves), saturated with spray (0.05% lindane in xylene as emulsion base): 3 died. 407

(3) Not to be applied directly to cattle; suckling pigs and lambs proved more resistant. 407

(4) Single spray of 1.5% lindane fatal to all cattle; 0.25% dilution tolerated. 407

b) Rabbits:

(1) Have withstood 10, but not 25, mg/k/day by cutaneous application. 451

(2) Painted daily for months with 1% in oil showed no irritation or other signs. 1977

c) Rat:

(1) Survived exposure to lindane in diet up to 1600 ppm for more than 1 year (at 800 ppm β-isomer all died within 10 weeks). Growth retarded on diets with 1600 ppm. 1015

(2) Toxicity of lindane deemed to be $\frac{1}{4}$th the chronic toxicity of DDT. 1016

(3) Reported to have tolerated 30 mg/k/day in the diet. 3064

(4) Weanlings on 600 ppm in diet (lard "solution") showed growth retard, weight loss, hyperactivity, 817
irritability and convulsions; initially many fatalities occurred among subjects. 816

(5) 10, receiving 25 mg/k/day cutaneously: 2 died after 6 and 7 days. 451

(6) Painted daily for 5 weeks (5% acetone solution): Retarded growth; no other signs. 1809

d) Guinea pig:

(1) 10 mg/k/day, cutaneous: Partly tolerated; weight loss, exhaustion; no nervous signs. 451

e) Fish:

(1) 11 varieties tropical fish, in aquaria aerated with household air containing vapors from continuous lindane space vaporizer: Heavy mortality; aquarium residues toxic to Musca; extreme nervousness, hypersensitivity among the signs. 2787

f) Man:

(1) Acceptable at 0.03-0.05% in salve for scabies 1 to 2 times per yr; 2 ounces of vanishing cream with 1% 2345
lindane have been employed by some without danger vs. scabies. 3371

(2) 15 subjects, single dose, 45 mg (as emulsion) orally (as vermifuge): 11 tolerated without effects; others 1240
developed various adverse symptoms, for example vertigo, epileptiform convulsions, nausea, pain. 1239

(3) Adults are said to have endured without effect 3 daily doses of 90 mg each. 3199

(4) Daily doses of BHC 40 mg (10-30% γ-isomer) tolerated through 8th dose when diarrhoea developed. Daily 40 mg doses of BHC (25-60% γ-isomer) tolerated; 90 mg doses after 5 days gave vertigo, diarrhoea, headache. Daily doses, 40 mg each, (60-85% γ-isomer) tolerated for 14 days; six 110 mg doses gave diarrhoea. 1823

(5) Highly purified lindane at 40 mg/day was tolerated without effects for 14 days; 100 mg doses well endured; 180 mg doses gave vertigo, diarrhoea. 1823

(6) Reported by some as irritating to skin; others claim it non-irritating to eyes, nose and throat. 1951,2698

3) Pharmacological, pharmacodynamic, physiological, etc; higher animals:

a) Lindane (γ-isomer) proved the most toxic of BHC isomers; toxicity varied with route, solvent and rate of absorption; for instance, ip LD_{50} for rat: In paraffin oil 35 mg/k, linseed oil 75 mg/k, cod liver oil 80 mg/k. 596

(1) Toxic impurities are suggested to explain some variations in toxicity. 1823

(2) More toxic (mg/k basis) for insects than for vertebrates: 2744,846

1928

Insecticide	LD_{50} (mg/k) For			
	Vertebrates*		Insects**	
	Topical	Injection	Topical	Injection
Lindane	300- 500	50 -75	0.4- 7.5	3-17
DDT	300-3000	12 -75	5 -30	5-60
Rotenone	Very High	0.4- 2.0	ca.30	6-15

*Frog, rat, rabbit, Guinea pig, cat, dog.

**Periplaneta, Musca, Aëdes, Calliphora.

(3) Lindane is a CNS stimulant yielding neurogenic signs, for instance, rise in blood pressure, fall 2203,582,2498
in heart rate; encephalogram of Grand Mal type. 687,451,2206

b) Symptoms:

(1) Hypersensitivity, excitation, equilibrium loss, ataxia, tremor, spasm, convulsions, paralysis; also 3199,2206
frequent urination, deep, rapid respiration; death in collapse, or after respiratory paralysis. In 451,89,1290
dogs (intramuscular, in oil), typical deep apathy, anorexia, weight loss with convulsions before 3277,1949
death. Human symptoms resemble animal symptoms. 353,2498,687

(2) Nervous signs yield to pentobarbital and in lesser degree to β-, and δ -isomers. 596,582,353,1290
3277,1949,89

(3) Acute poisoning: Predominance of nervous signs: Dogs, iv 3.3 mg/k in alcohol, underwent 687
immediate convulsions; convulsions came in 15-40 minutes after 100 mg/k orally; barbiturates, 2498
curare and cervical spinal section, forestalled convulsions. Convulsant dose dogs = 1 mg/k; rabbits = 1.75 mg/k.

c) Absorption:

(1) Via gastro-intestinal, dermal, respiratory routes. Preferentially deposited in fat, localizing chiefly 708
in brain, kidney and muscle. 1928

d) Excretion:

(1) Via urine chiefly; rapid elimination (swifter in ♂), rapidly metabolized. 1967,1058,708
1951,1928,3169

e) Mode of action:

(1) Essentially unknown; Theory: Blockage of (or competition with) meso-inositol in cell metabolism. 353

Inositol, however, fails to alleviate symptoms in young rats; O_2 uptake, in vitro, of brain preparations was uninfluenced by inositol.

(2) Inhibits cleavage and development in echinoderm eggs; effect not relieved by inositol. 507

(3) Inhibits ciliary movement in Glaucoma piriformis (Protozoa); unrelieved by inositol.

(4) Antagonizes (in mammals) the convulsant action of metrazol and coramine. 1500

f) Pathology:

(1) DDT-like. Rat, 100 ppm in diet showed histological changes liver, kidney (at 10 ppm no signs). 1015,1016,686
Liver enlargement, color change, focal necrosis; hepatic cell swelling, atrophy, fatty degener- 407,3330,1949

ation, congestion. Dog: Repeated intra-muscular doses brought fat deposit of lindane (liver, skeletal muscle, nerves, renal tubules); bladder congestion, epithelial sloughing; hemorrhage (intestines, lungs heart); oedema (brain, spinal cord). 1083,89

(2) Following lindane vapor exposures, Man: Urticaria (allergic response?); nephritis. 582,584

4) Phytotoxicity; effects on Plants: (Also see BHC)

a) Not considered high in phytotoxic hazard if application directions are rigidly adhered to. Formulation 2120
and solvents may influence. Residues on plant surfaces last ca. 4 days. 129

(1) Tainting properties for plant products: Less than for BHC, q.v.; "off-flavor," and odor detected (2 lbs/ 721
acre [application excessive]) in tomato, potato, radish, carrot, etc. 2120

(2) Stable in the soil; 80% recoverable after 18 months. 2898

(3) Soils originally containing 2%, after 18 months inhibited root growth of sprouting seeds; root growth inhibition at 0.002%. 2898

(4) Malformation, stunting, distortion of radicle and plumule of germinating seeds. 2740

b) Colchicine-like action on plant cells (Allium cepa root tip cells) with arrest of mitosis in metaphase, 2740,528
collapse of the achromatic figure with resultant polyploidy, aneuploidy, multinucleate cells and other 506,507
cytological-monstrosities.

c) Effect of lindane and BHC in the inhibition of growth of three plant species whose germination is unaffected by seed treatment with the insecticides: Incubator tests 3 days duration at 24° and 30°C: 2215

Insecticide	g/k Seed	% Growth Inhibition Of		
		Wheat	Rye	Barley
Lindane	0.15	16	—	—
"	.30	20	29	—
"	.60	37	47	29
"	.90	—	—	28
"	1.20	—	71	51
BHC	.15	63	—	—
"	.30	75	75	51
"	.60	77	80	60
"	.90	—	—	—
"	1.20	—	85	60

d) As a seed dressing: Sugar beet less sensitive to lindane than grains and corn. 2215

(1) No influence on germination of corn treated at 0.3-2.4 g/k. 2215

e) Lindane had no effect on treated wheat in 3 months storage (BHC impaired germination and growth in 1 month). 2215

f) Rye: Undamaged when lindane treated and stored 3 months (BHC harmed both germination, growth). 2215

g) Sugar beet seed treated with lindane: Undamaged in 4 months storage (BHC caused poor stands after 1 month storage and heavy damage after 4 months storage). 2215

5) Toxicity for insects:

a) One of the most potent insecticides thus far developed; no insect is known which can withstand appreciable 846
doses. LD_{50} (topical) varies roughly (0.4-57 mg/k) depending on species. Most insecticidal by far of the 2822
BHC isomers, being 1000 times as toxic to Sitophilus granarius as the technical isomer mixture. Insect- 2227
icidal activity of BHC is due entirely to the γ-isomer (lindane) content.

(1) Compared with the δ-isomer, lindane is 94% more insecticidal for Macrosiphum, 98% more for 2822
Epilachna, 99% more for Sitophilus, 99.9% more for Heliothrips. 2227,2040

(2) Fumigant activity is good (due to relatively high vapor pressure;) exposure of 1 hr. to 1 day, depending on species, is sufficient to kill; lethal time declines with temperature rise, Q_{10} for fumigant toxicity, in range 59°-86°F, = ca. 2. 353

(3) Resistance to lindane, both ad hoc, and as a concomitant of resistance to DDT and other compounds, 353,2231
has been noted in biotypes subjected to selection by exposure. 2098,373,371

(4) Comparative order of toxicity for insects; lindane, DDT, chlordane: 3015

Stomach: lindane > DDT > chlordane.
Contact: DDT > lindane > chlordane.
Fumigation: chlordane > lindane > DDT.

b) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti (adult) ♂	Contact Spray	LD_{50}	3.0 mg/k	Insect in flight in mist laden air.	693,696
Aëdes aegypti (") ♀	Contact Spray	LD_{50}	3.5 mg/k	" "	693
Aëdes aegypti (")	Topical	LD_{50}	2.0 mg/k		696
Agrotis orthogonia (larva)	Residual	L $Deposit_{50}$	5.5 µg/cm^2		350
Anopheles quadrimaculatus (larva)	Medium	MLD_{100}	0.05 ppm	62% kill at 0.025 ppm.	2020
Anopheles quadrimaculatus (adult) ♂	Topical	LD_{50}	0.0085 µg/insect	4 day old adults.	2051
Anopheles quadrimaculatus (") ♀	Topical	LD_{50}	0.011 µg/insect	"	2051
Anopheles quadrimaculatus (") ♂	Topical	LD_{90}	0.032 µg/insect	"	2051
Anopheles quadrimaculatus (") ♀	Topical	LD_{90}	0.042 µg/insect	"	2051
Anthonomus grandis (adult)	Fumig	LC_{50}	233.5 mg/l		2276
Apis mellifera (adult)	or	LD_{20}	0.03 µg/bee	Suspension in sugar + water medium.	3247
Apis mellifera (")	or	LD_{50}	0.08 µg/bee	" "	3247
Apis mellifera (")	or	LD_{95}	0.54 µg/bee	" "	3247
Apis mellifera (")	or	LD_{20}	0.026 µg/bee	" "	1718
Apis mellifera (")	or	LD_{50}	0.079 µg/bee	" "	1718
Apis mellifera (")	or	LD_{90}	0.35 µg/bee	" "	1718

Insect	Route	Dose	Dosage	Remarks	
Apis mellifera (adult)	Contact Spray	L Deposit$_{20}$	0.77 μg/cm^2	Aqueous emulsion spray.	1718
Apis mellifera (")	Contact Spray	L Deposit$_{50}$	0.85 μg/cm^2	" .	1718
Apis mellifera (")	Contact Spray	L Deposit$_{90}$	0.986 μg/cm^2	" .	1718
Apis mellifera (")	Residual	L Deposit$_{100}$	0.0028 mg/cm^2	Exposure: 1 hour.	1718
Apis mellifera (")	Residual	L Deposit$_0$	0.000074 mg/cm^2	" : " .	1718
Blattella germanica	Contact Spray	L Deposit$_{50}$	2.8 μg/cm^2		356
Blattella germanica	Contact Dust	L Deposit$_{50}$	0.8 μg/cm^2	Insect dusted; clean cage.	2357
Blattella germanica	Environment	L Deposit$_{50}$	0.2 μg/cm^2	Cage dusted; insect placed in.	2357
Blattella germanica (adult) ♀	inj	LD_{50}	1.01 μg/g	Chlordane non-R strain.	431
Blattella germanica (") ♀	inj	LD_{90}	2.57 μg/g	" .	431
Blattella germanica (") ♀	inj	LD_{50}	23.13 μg/g	Chlordane-R (Corpus Christi) degree-R = 22.72.	431
Blattella germanica (") ♀	inj	LD_{90}	75.02 μg/g	" degree-R = 29.19.	431
Blattella germanica (") ♂	Dipping	LC_{50}	10.3 mg/l	Chlordane non-R strain.	1259
Blattella germanica (") ♂	"	LC_{90}	15.5 mg/l	" .	1259
Blattella germanica (") ♀	"	LC_{50}	24.2 mg/l	" .	1259
Blattella germanica (") ♀	"	LC_{90}	43.0 mg/l	" .	1259
Blattella germanica (") ♂	"	LC_{50}	59.5 mg/l	Chlordane-R strain. Degree R = 5.7.	1259
Blattella germanica (") ♀	"	LC_{50}	94 mg/l	" " = 3.8.	1259
Blattella germanica (") ♂	"	LC_{90}	76 mg/l	" " = 4.9.	1259
Blattella germanica (") ♀	"	LC_{90}	185 mg/l	" " = 4.3.	1259
Choristoneura fumiferana (larva)	Residue	L Deposit$_{50}$	1.9 μg/cm^2		350
Chrysops discalis (adult)	Topical	LD_{50}	4 μg/fly		2707
Chrysops discalis (")	Topical	LD_{90}	35 μg/fly		2707
Cimex lectularius	Contact Spray	LD_{50}	23 μg/insect	In white (P31) oil.	413
Cimex lectularius	Contact Spray	LD_{50}	6 mg/k	"	413
Cimex lectularius	Contact Spray	LC_{50}	0.051% conc.	At 0.36 mg spray/cm^2; in P31 oil.	413,418,419
Diataraxia oleracea (larva)	Contact Spray	LD_{50}	13 μg/larva	Wgt. of insect: 0.32 g.	3245
Diataraxia oleracea (")	Contact Spray	LD_{50}	26 μg/larva	" : 0.42 g.	3245
Diataraxia oleracea (")	Contact Spray	LD_{50}	59 μg/larva	" : 0.56 g.	3245
Ephestia kühniella	Medium	LC_{50}	10 ppm	Mixed with grain.	353
Fannia canicularis (3 day adult) ♀	Topical	LD_{50} 24 hr.	0.76 μg/fly	Av. wgt. fly: 7.35 mg; acetone sol.	1981
Fannia canicularis (") ♂	Topical	LD_{50} 24 hr.	0.39 μg/fly	" : 6.89 " ; acetone sol.	1981
Heliothis ononis (larva)	Residue	L Deposit$_{50}$	23.0 μg/cm^2		350
Heliothrips hemorrhoidalis	Spray	LC_{50} 24 hr.	0.0001% conc.		2230
Locusta migratoria migratorioides (adult)	Topical	LD_{50} 96 hr.	3.89± 0.21 μg/insect	In tractor vaporising oil.	1585
Locusta migratoria migratorioides (")	Topical	LD_{50} 96 hr.	3.69 μg/g	" .	1585
Locusta migratoria migratorioides (adult)	Topical	LD_{95}	12.9± 2.09 μg/insect	" .	1585
Locusta migratoria migratorioides (")	Topical	LD_{95}	12.2 μg/g	" .	1585
Melanoplus differentialis	Topical	LD_{50}	1.6; 3.4 μg/g	In acetone solution.	3266,3267
Melanoplus differentialis	or	LD_{50}	6.7 μg/g	As deposit on leaves.	3266,3267
Melanoplus differentialis (1st, 2nd instar)	Contact Spray	LD_{50}	0.08 Lb/acre	Emulsion from miscible concentrate in oil solution.	1102
Musca vicina (adult)	Topical	LD_{50}	0.028 μg/fly		425
Musca domestica (adult) ♀	Topical	LD_{50}	0.01 μg/fly	Measured drop method; acetone sol.	1981
Musca domestica (adult)	Topical	LD_{50} 24 hr.	0.024 μg/fly	.022 mg/cc (LC_{50}) lindane alone; rel. tox. = 1.0.	3130
Musca domestica (adult)	Topical	LD_{50} 68 hr.	0.017 μg/fly	.016 mg/cc (LC_{50}) " "	3130
Musca domestica (")	Topical	LD_{50} 24 hr.	0.032 μg/fly	.029 mg/cc With Aroclor 5460; rel tox. 76.	3130
Musca domestica (")	Topical	LD_{50} 68 hr.	0.021 μg/fly	.0195 mg/cc " " 82.	3130
Musca domestica (")	Topical	LD_{50} 24 hr.	0.03 μg/fly	80°F; Laboratory strain.	371
Musca domestica (")	Topical	LD_{50} 24 hr.	> 10.0 μg/fly	80°F; after 46 generations exposure.	371
Musca domestica (")	Topical	LD_{50} 24 hr.	0.01 μg/fly	60°F; Laboratory strain.	78,371,2098
Musca domestica (")	Topical	LD_{50} 24 hr.	0.08 μg/fly	60°F; Bellflower (DDT-R) strain.	78,371,2098
Musca domestica (")	Topical	LD_{50} 24 hr.	0.25 μg/fly	60°F; Pollard (DDT-R) strain.	371
Musca domestica (")	Topical	LD_{50} 24 hr.	0.06 μg/fly	Riverside strain (DDT-R).	2098,78
Musca domestica (")	Topical	LD_{50} 24 hr.	0.05 μg/fly	Ontario and San José (DDT-R) strains.	2098,78
Musca domestica (")	Contact Spray	LC_{50} 24 hr.	0.046 mg/cc of spray	Turntable method.	2033
Musca domestica (")	Topical	LD_{50} μg/g	5.52	DDT-I strain; in acetone sol.	373
Musca domestica (")	Topical	LD_{50} 24 hr.	2.1 μg/g	DDT-W strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	2.2 μg/g	DDT-III strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	3.75 μg/g	Methoxy-I strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	33.4 μg/g	Lindane-I strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	8.56 μg/g	Multi-I strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	2.8 μg/g	Dieldrin-I strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	2.2 μg/g	Chlordane-I strain; in acetone solution.	373
Musca domestica (")	Topical	LD_{50} 24 hr.	1.7 μg/g	Lab-I strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	2.2 μg/g	Lab-II strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	7.7 μg/g	Pyro-I (Pyrethrin) strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	25.0 μg/g	Multi-III strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	7.38 μg/g	Multi-IV strain; " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	5.3 μg/g	Multi-II " .	373
Musca domestica (larva)	Medium	LC_{50}	44 ppm	As judged by pupal emergence 8 ppm.	2179,2180
Pediculus humanus corporis	Contact Spray	LD_{50}	3 μg/insect; 1.5 mg/k	in white oil (P31).	413
P. humanus corporis	Contact Spray	LC_{50}	0.02% conc.	Sprayed at 0.36 mg/cm^2; in P31 oil.	413,418,419
Periplaneta americana ♂ (adult)	inj	LD_{50} 96 hr.	0.8 μg/g	In xylene, acetone, deobase, alcohol 10:10:75:5 parts.	558
Periplaneta americana ♀ (")	inj	LD_{50} 96 hr.	4.4 μg/g	" "	558
Prodenia eridania (large larva)	or	LD_{50}	0.031 mg/g	Given by leaf sandwich method.	3017
Prodenia eridania (0.012 g larva)	Fumig	Av kill % 2 da	35%	Exposed at saturation; 24-25°C.	3017
Prodenia eridania (0.7 g larva)	Contact Dusts	L Deposit$_{32}$ 2 da	0.58 mg/cm^2	As 1% dust in pyrophyllite.	3017
Protoparce sexta (5th instar larva)	Topical	LD_{50}	206 μg/larva	Large insects; 5.4 (4.1-7.5) g.	1306
Protoparce sexta (")	Topical	LD_{90}	1235 μg/larva	" " .	1306
Protoparce sexta (")	or	LD_{50}	209 μg/larva	" " .	1306
Protoparce sexta (")	or	LD_{90}	398 μg/larva	" " .	1306
Sitophilus granarius	Medium	LC_{50}	0.1 ppm	Mixed with grain.	353
Tribolium confusum	Medium	LC_{50}	3.0 ppm	" .	353
Paratetranychus citri	Spray	LC_{50} 24 hr.	1.0%		2230
Boophilus microplus ♀	Dipping	LC_{50}	40.0 ppm		1541

c) Lindane as a vapor; toxicity for insects:

(1) Vs. Musca domestica, adult, DDT-R, DDT-non-R strains: 3320

Strain (Biotype)	Lethal Time$_{50}$ (Minutes)	
	Vapor (At Saturation)	On Residues
non-R	25	10.9
Orlando No 1	58	16.4
LDD	173	65.6
Ballard	316	229.3

(2) Concentrations and exposure times required to give various percentages of mortality for various insects exposed in Peet-Grady chamber: 3007

Insect	Exposure (Minutes)	% Mortality At	
		0.6 μg/l (24°C)	1.19 μg/l (30°C)
Periplaneta americana (adult)	60	21	33
"	240	48	72
Tribolium confusum (adult)	60	12	67
"	120	38	72
"	180	56	88
Acanthoscelides obtectus (adult)	15	80	95
"	30	96	100
Musca domestica (adult)	2	59	75
"	5	79	97
"	10	90	100
Aëdes aegypti (adult)	2	99	100
"	5	100	100
"	10	100	100

(3) At a concentration of 0.08 g/m^3, lindane was non-corrosive, non-toxic for mammals and, with absolute airtightness unnecessary, effectively protected stored materials against: Sitophilus granarius, Sitophilus oryzae, Rhizopertha dominica, Tenebrioides mauritanicus, Oryzaephilus surinamensis, Stegobium paniceum, Tenebrio, Tribolium, Gnathocerus, Corynetes, Necrobia, Dermestes, Attagenus, Trogoderma, Anthrenus, Acanthoscelides obtectus, Laemphloeus, Ptinus, Niptus, Carpophilus, Lasioderma serricorne, Ephestia kuhniella, Ephestia elutella, Sitotraga cerealella, Tinea granella. 303

At 0.8 ppm: Completely protected wheat for at least 6 months vs. Sitophilus granarius. 521

d) Comparative toxicity for insects; lindane and other insecticides:

(1) Vs. Melanoplus differentialis and Locusta migratoria migratorioides; adult insects; by various routes: 3267 1102,1585

Insecticide	M. differentialis			L. migratoria migratorioides			
	LD$_{50}$			****LD$_{50}$ Topical 96 hrs.		LD$_{95}$ Topical	
	*Contact (μg/g)	**Contact (lb/acre)	***Oral μg/g	μg/insect	μg/g	μg/insect	μg/g
Lindane	1.6;3.4	.08	6.6;6.7	3.89± .21	3.69	12.9± 2.1	12.2
Aldrin	1.8	.04	2.3	–	–	–	–
BHC	–	.04	–	–	–	–	–
Chlordane	9.8;16.3	.49	12.0;21.8	20.4± 1.05	19.3	110.0±30.9	104.0
DDT	>3300;9380	–	††1170;>1350;2579	140.0± 7.6	133.0	258.0± 18.6	245.0
Dieldrin	1.4	.03	3.7	–	–	–	–
Heptachlor	1.6;2.6	–	4.4;6.0	–	–	–	–
Toxaphene®	61.0;73.9	.91	75.0;91.5	40.2± 2.9	38.1	123.0± 16.9	116.0
DNOC	–	–	–	10.4± 0.1	9.9	19.3± .897	18.3
Parathion (tech)	0.7;0.8	.05	6.0-8.9	–	–	–	–
Methyl parathion	–	–	–	0.94± 0.1	0.89	2.3± .52	2.2
HETP	18.4	–	–	–	–	–	–
TEPP	4.4	–	–	–	–	–	–

*Solutions in dioxane, acetone, or ethanol.
**Contact emulsion sprays from emulsifiable concentrates; 1st and 2nd instar nymphs.
***As deposits on leaves.
****In tractor vaporising oil + cyclohexanone (9:1).
††As colloidal suspension, directly to mouth parts.

(2) Lindane and other compounds, vs. Artemia salina (Crustacea) as a test organism for insecticide bio-assay. Time required for fall of Artemia to bottom of water column due to cessation of swimming movements: 2251

Insecticide	Time (Min) For Fall At		
	1 ppm	0.1 ppm	0.01 ppm
Lindane	45-60	60-120	60-120
Chlordane	60-120	120-135	120-180

Insecticide	Time (Min) For Fall At		
	1 ppm	0.1 ppm	0.01 ppm
Methoxychlor	45-60	45-60	45-60
Toxaphene®	45-60	90-120	18 hrs.
DDT	60	60	60-120
Acetone control 1:100	25-48 hrs.		
Water control	26-50 hrs.		

(3) Lindane and other substances as stomach poisons for certain Lepidoptera; Diataraxia oleracea (last instar larva), Prodenia eridania (large larvae 0.7 g. wgt.), Protoparce sexta (5th instar larvae 5.4 (4.1-7.5) g. wgt.). Oral administration: 3245 3017 1306

Insecticide	P. sexta		P. eridania*	D. oleracea**		
	LD$_{50}$ (μg/larva)	LD$_{90}$ (μg/larva)	LD$_{50}$ (μg/g)	LD$_{50}$ (μg/larva) At Larval Wgt. Of		
				0.32 g	0.42 g	0.56 g
Lindane	209	398	31	13	26	59
Chlordane	—	—	130	—	—	—
Endrin	9.9	49	—	—	—	—
Isodrin	15.3	138	—	—	—	—
Toxaphene®	143	6,025	—	—	—	—
DDD	878	3,192	—	—	—	—
DDT	4,416	28,040	31	4.5	12	33
Parathion	15.7	54	—	2.6	3.4	4.6
Malathion	365	1,621	—	—	—	—
TEPP	—	—	—	43	69	112
Acid Lead arsenate	—	—	290	66	78	91

*Oral administration by leaf sandwich method.
**Oral administration by leaves treated in settling tower.

(4) Lindane and other insecticides, contact toxicity for certain larval Lepidoptera: Choristoneura fumiferana, Heliothis ononis, Agrotis orthogonia, Protoparce sexta, Prodenia eridania: 350 3017,1306

Insecticide	Lethal Deposit$_{50}$ (μg/cm^2)			*P. sexta (Topical)		**P. eridania	
	C. fumiferana	H. ononis	A. orthogonia	LD$_{50}$ μg/larva	LD$_{90}$ μg/larva	Deposit mg/cm^2***	Av. kill, 2 days
Lindane	1.9	23	5.5	206	1235	0.58	32%
Chlordane	140.0	non-toxic	18	—	—	0.55	2%
Endrin	—	—	—	42	219	—	—
Isodrin	—	—	—	87	490	—	—
Dieldrin	—	—	—	482	2559	—	—
Aldrin	—	—	—	487	1359	—	—
Heptachlor	—	—	—	1058	4005	—	—
DDT	0.3	7	80	≫4000	9897****	0.53	40%
DDD	—	—	—	2622	9813	—	—
Toxaphene®	—	—	—	1363	5778	—	—
Parathion	—	—	—	52	183	—	—
Malathion	—	—	—	481	1276	—	—
DNOC	4.0	16	7.5	—	—	—	—
Nicotine	42	400	negative	—	—	—	—
Pyrethrins	0.05	4	8.2	—	—	—	—

*Large larvae, 5th instar 5.4(4.1-7.5)g. Topical application.
**Large larvae, 0.7g wgt.
***Applied as 1% dusts in pure pyrophyllite.
****Medium larvae 2.5(1.2-4.0)g, 3rd, 4th instars.

(5) Lindane and other insecticides vs. certain Diptera: Musca domestica, Fannia canicularis, Chrysops discalis, Anopheles quadrimaculatus; Adult insects: 78,1981 2707,2051

Insecticide	Musca			Fannia****		Chrysops		Anopheles			
	*Topical LD$_{50}$ 24 Hrs. (μg/fly) ♀	**Contact Spray (mg/cc) For 50% Kill At 24 Hrs.	***KD 10 Min (%)	*Topical LD$_{50}$ 24 Hrs. (μg/fly)		Topical (μg/fly)		†Topical (μg/insect)			
				♀	♂	LD$_{50}$	LD$_{90}$	LD$_{50}$		LD$_{90}$	
								♂	♀	♂	♀
Lindane	0.01	0.046	0	0.76	0.39	4	35	.0085	.011	.032	.042
Aldrin	—	0.056	0	—	—	40	170	—	—	—	—
Chlordane	—	0.25	0	—	—	60	650	.105	.24	.19	.46
DDD (p,p')	0.1	—	—	—	—	—	—	.041	.1	.098	.22
DDT (p,p')	0.02;.033	0.35	0	2.8	1.3	20	250	.02	.066	.045	.13
Dieldrin	0.031	0.017	0	0.003	0.0026	20	950	.009	.023	.022	.048
Dilan	—	0.72	ca. 30	—	—	—	—	—	—	—	—
Endrin	—	—	—	—	—	9	80	—	—	—	—

(5) Lindane and other insecticides vs. certain Diptera: Musca domestica, Fannia canicularis, Chrysops discalis, Anopheles quadrimaculatus; Adult insects: 1981,78 2707,2051

Insecticide	Musca			Fannia****		Chrysops		Anopheles			
	*Topical LD$_{50}$ 24 Hrs. (μg/fly) ♀	**Contact Spray (mg/cc) For 50% Kill At 24 Hrs.	***KD 10 Min (%)	*Topical LD$_{50}$ 24 Hrs. (μg/fly)		Topical (μg/fly)		Topical †(μg/insect)			
				♀	♂	LD$_{50}$	LD$_{90}$	LD$_{50}$		LD$_{90}$	
								♂	♀	♂	♀
Heptachlor	0.03	0.052	0	—	—	40	200	—	—	—	—
Isodrin	—	—	—	—	—	60	170	—	—	—	—
Methoxychlor	0.068	—	—	0.14	0.12	30	90	.035	.1	.078	.22
Q-137	—	—	—	—	—	120	400	—	—	—	—
Toxaphene®	0.2	0.68	0	—	—	180	480	.15	.29	.29	.5
Chlorthion®	0.33	—	—	0.035	0.022	65	420	—	—	—	—
Diazinon	0.092	—	—	0.098	0.054	90	360	—	—	—	—
Dipterex®	—	—	—	—	—	90	910	—	—	—	—
EPN®	—	—	—	—	—	48	120	—	—	—	—
Malathion	0.56	0.48	0	0.10	0.06	130	330	.0087	.0095	.019	.022
Methyl parathion	—	0.025	0	—	—	—	—	—	—	—	—
Parathion	—	0.02	0	—	—	—	—	—	—	—	—
TEPDP‡	—	0.69	0	—	—	—	—	—	—	—	—
TEPP	—	0.069	ca. 70	—	—	—	—	—	—	—	—
Isolan	—	1.15	100	—	—	—	—	—	—	—	—
Pyrolan	—	5.5	100	—	—	—	—	—	—	—	—
Allethrin	—	1.5	100	—	—	—	—	.0029	.008	.013	.041
Pyrethrins	1.0	ca. 1	100	0.24	0.44	—	—	—	—	—	—
Para-oxon	2.6 (μg/g)	—	—	—	—	—	—	—	—	—	—

‡Tetrapropyl dithiopyrophosphate.
*Insecticides in acetone solution; measured drop method.
**Turntable modification of Peet-Grady Method.
***At the LC$_{50}$ dosage.
****Av. wgt. ♂ 6.89 mg, ♀ 7.35 mg.
†Insecticides in ethanol solution.

(6) Lindane, others, "Knockdown" in residual application tests vs. DDT-R, DDT-non R Musca domestica: 78

Insecticide	Bellflower strain minutes for		San José strain minutes for		Laboratory strain minutes for	
	KD$_{50}$	KD$_{100}$	KD$_{50}$	KD$_{100}$	KD$_{50}$	KD$_{100}$
Lindane at 10 mg/ft^2	11	15	16	20	13	20
DDT at 100 mg/ft^2	720	2880	420	1440	91	152
Methoxychlor at 100 mg/ft^2	255	360	56	108	37	67
Heptachlor at 10 mg/ft^2	40	52	48	60	44	51

(7) Lindane and other compounds by measured drop tests vs. Musca domestica, DDT-R, and DDT-non R biotypes: 78

Insecticide	LD$_{50}$ 24 Hrs. (μg/fly) For				
	Bellflower*	San José*	Ontario*	Riverside*	Laboratory*
Lindane	0.08	0.05	0.05	0.06	0.01
DDT	10	.7	.5	.5	.02
DDD	20	—	—	—	.1
Methoxychlor	1	.3	.3	.3	.07
Toxaphene®	.6	.4	.5	.5	.2
Heptachlor	.06	.07	.07	.07	.03
Pyrethrins	1	2	2	2	1

*Strain or biotype.

(8) Relative effectiveness (compared to DDT) of Lindane and other compounds vs. adult Anopheles quadrimaculatus (4 day adults) tested by topical application of toxicants in ethanol solution: 2051

Insecticide	Relative Effectiveness (DDT=1) At			
	LD$_{50}$		LD$_{90}$	
	♂	♀	♂	♀
Lindane	2.4	6.0	1.4	3.1
Toxaphene®	.13	.23	.16	.26
Chlordane	.19	.28	.24	.28
DDD (p,p')	.49	.66	.46	.59
Methoxychlor	.57	.66	.58	.59
DDT (p,p')	1	1	1	1
Dieldrin	2.2	2.9	2.0	2.7
Allethrin	6.9	8.3	3.5	3.2
Malathion	2.3	7.0	2.4	5.9

(9) Lindane and other insecticides in control of Musca domestica larvae (maggots); as emulsions applied to breeding media; laboratory tests: 1326

Insecticide	% Mortality At					
	50 mg/k*	20 mg/k	15 mg/k	10 mg/k	5 mg/k	2 mg/k
Lindane	—	99.5	—	60	—	—
DDT	100	—	—	—	—	—
Methoxychlor	25	—	—	—	—	—
Toxaphene®	100	100	—	100	75	0
Chlordane	—	—	100	—	—	75
Aldrin	—	—	100	100	100	97.5
Dieldrin	—	100	—	100	100	94
Heptachlor	—	100	—	—	100	90
Dilan	99.5	100	—	100	5	—

*Milligrams per kilogram of medium.

Results in field less encouraging; adult flies not significantly decreased in number, although control of larvae was obtained in such breeding places as could be detected.

(10) Residual effectiveness of Lindane and other substances incorporated (at 20% [dry wgt basis]) in various surface coatings vs. Musca domestica: 267

Insecticide	Vehicle (Surface Coating)	Time (Minutes) For KD$_{50}$		
		Initial	After Stated Interval (→)	Interval (weeks)
Lindane	Urea-formaldehyde	13	16	6
DDT	"	16	10	28
Chlordane	"	60	41	7
Toxaphene®	"	48	35	12
DDD	"	28	25	17
Pyrethrum	"	18	2,11,23,52	8,14,15,17 days
Lindane	Nitrocellulose	39	20	30
DDT	"	60	17	35
Chlordane	"	76	28	30
Toxaphene	"	55	26	12
Lindane	Polymerized diolefins	20	23	6
DDT	"	21	32	6
Chlordane	"	71	29	30

(11) Lindane and other compounds vs. Periplaneta americana (adult): 558,267

Insecticide	*LD$_{50}$ 96 Hrs., Injection (µg/g)		LD$_{50}$ ♀ / LD$_{50}$ ♂	(On** Treated Wall Coatings)	
	♂	♀		KD$_{50}$ (Hrs.)	KD$_{100}$ (Hrs.)
Lindane	0.8	4.4	5.5	1	1.5
Dieldrin	1.0	5.0	5.0	—	—
DDT	4.5	20.0	4.4	24	48
DDD	—	—	—	>48	—
Toxaphene®	25.0	80.0	3.2	>48	—
Chlordane	26.0	52.0	2.0	15	18
Methoxychlor	7.0	18.0	2.5	—	—

*Toxicants dissolved in xylene + acetone + deobase + ethanol, 10:10:75:5.
**Toxicants incorporated at 50% of dry wgt. in urea-formaldehyde wall coating.

(12) Toxicity of Lindane and other substances for Blattella germanica (adult) chlordane-R (Corpus Christi) and chlordane-non R biotypes: 431 1259

Insecticide		By Injection (µg/g)						By Dipping (Lindane mg/l, others cc/l)					
		Non-R		R		Resistance At		Non-R		R		Resistance At	
		LD$_{50}$	LD$_{90}$	LD$_{50}$	LD$_{90}$	LD$_{50}$	LD$_{90}$	LD$_{50}$	LD$_{90}$	LD$_{50}$	LD$_{90}$	LD$_{50}$	LD$_{90}$
Lindane	♂	—	—	—	—	—	—	10.3	15.5	59.5	76	5.7	4.9
"	♀	1.01	2.57	23.13	75.02	22.72	29.19	24.2	43.0	94	185	3.8	4.3
Aldrin	♀	26.46	70.06	127.61	1113.6	4.82	15.89	—	—	—	—	—	—
Chlordane	♂	—	—	—	—	—	—	.0034	.0063	.38	2.1	111.7	333.3
"	♀	81.29	144.27	1117.5	4648.8	13.76	32.22	.0165	.0476	4.55	14.87	275.7	312.3
Dieldrin	♀	6.59	17.35	68.37	502.49	10.37	28.54	—	—	—	—	—	—
Heptachlor	♀	9.07	19.85	174.21	1509.3	19.21	76.04	—	—	—	—	—	—
TEPP	♂	—	—	—	—	—	—	.0575	.11	.112	.165	1.9	1.5
"	♀	—	—	—	—	—	—	.153	.395	.265	.512	1.7	1.2

(13) Lindane and other insecticides in protection of stored products; toxicities for certain stored products insects; toxicants mixed with grain: 353 303 114 399 1343

Insecticide	LC$_{50}$ (ppm) For		
	Sitophilus granarius	Ephestia kühniella	Tribolium confusum
Lindane	0.1	10	3
DDT	16	860	16
Chlordane	1.3	36	0.2
Hexachloropropene	450	4	10

(a) 3-6 ppm. protected seeds without risk of phytotoxicity (lindane). Wheat may be treated with lindane dusts against grain beetles. France permits use of lindane (99% pure) in cereal and leguminous products, for human use, at rate of 0.5 g/100 k (as a maximum) providing there is complete uniformity by mixing and that the resulting flour or meal contains less than 1 ppm of lindane.

(b) Vs. Sitophilus granarius, lindane is 900 times more toxic than α-BHC, 5500 times more toxic than δ-BHC; β-BHC is virtually non-toxic.

(14) Lindane and other compounds; toxicity of vapors for resistant biotypes of Musca domestica; Orlando 3320

No. 1 = strain exposed only to DDT with high resistance for DDT and some cross resistance for lindane, dieldrin, chlordane; LDD = a biotype collected from dairies where DDT, dieldrin, lindane, would not control, resistance maintained by continuous exposure to residues in adult cages; Ballard = a wild collected biotype from a dairy where space and residual lindane was relatively ineffective:

Biotype	Lethal Time$_{50}$ (Minutes) For				
	Vapors				DDT On Residues
	Lindane	Chlordane	Dieldrin	Aldrin	
Non-R	25	33	40	< 15	9
Orlando No. 1	58	69	110	23	ca1440
LDD	173	347	550	158	> 240
Ballard	316	380	550	96	343.4

(15) Lindane and other insecticides vs. Anasa tristis; topical application as acetone solutions: 3376

Insecticide	% Mortality 72 Hrs. At					Speed of Action At Lowest Dosage, Topical, Giving 90% Or Better Kill In 72 Hrs.				
	32 µg/g	64 µg/g	128 µg/g	256 µg/g	512 µg/g	Dosage µg/g	% Kill At 12 hrs.	24 hrs.	48 hrs.	72 hrs.
Lindane	83.3	100	100	100	100	64	—	80	100	100
Parathion	100	100	100	100	100	6	3.3	33.3	76.7	90
Aldrin	—	93.3	100	100	100	64	—	23.3	76.7	93.3
Endrin	—	—	100	100	100	128	6.7	20	86.7	100
EPN®	—	—	100	100	100	128	10	26.7	76.7	100
Heptachlor	—	83.3	90	100	100	128	10	50	80	90
Isodrin	—	—	90	100	100	128	0	10	63.3	90
Dieldrin	—	—	70	100	100	256	0	70	96.7	100
Chlordane	—	—	36.7	80	90	512	—	6.7	73.3	90
Toxaphene®	—	—	16.7	66.7	82	—	—	—	—	—
DDT	—	—	20	30	76.7	—	—	—	—	—

(16) Lindane and others; speed of toxic action vs. Macrosiphum pisi on young Vicia faba plants as dusts (in talc) applied in dusting tower: 520

Insecticide	Concentration (%)	°F	Time Required For 50% Kill (hrs:min.)	98% Kill (hrs:min.)
Lindane	1	72	0:56	1:54
Nicotine	1	72	0:15	1:12
"	3	72	0:12	0:50
TEPP	0.18	74	0:20	0:56
Rotenone	5	72	0:47	1:23
DDT	5	72	0:57	1:45
Parathion	1	70	1:8	1:43
"	2	70	1:21	1:53
Methoxychlor	10	75	2:1	5:34
DDD	5	72	2:34	4:35
Aldrin	1	75	3:44	7:32
Dieldrin	1	75	4:7	6:43
EPN®	0.86	74	5:26	8:6
Chlordane	5	72	9:24	18:8
Toxaphene®	5	72	13:20	19:1
Pure Talc		67-72	13:28	23:51

(17) Lindane and other insecticides vs. Pediculus humanus corporis and Cimex lectularius; contact sprays in P31 oil applied at deposit of 0.36 mg spray/cm^2: 418 414,413

Insecticide	Cimex			Pediculus		
	LC$_{50}$ (%)	LD$_{50}$ (µg/insect)	LD$_{50}$ mg/k	LC$_{50}$ (%)	LD$_{50}$ (µg/insect)	LD$_{50}$ (mg/k)
Lindane	0.05	.023	6	0.02;016	0.003	1.5
Lauseto Neu	0.2	—	—	0.1	—	—
DDT	0.5	.25	63	0.3	.054	27
Methoxychlor	0.5	—	—	0.9	—	—

Insecticide	Cimex			Pediculus		
	LC$_{50}$ (%)	LD$_{50}$ (μg/insect)	LD$_{50}$ mg/k	LC$_{50}$ (%)	LD$_{50}$ (μg/insect)	LD$_{50}$ (mg/k)
DDD	1.2	–	–	0.9	–	–
DFDT	5.0	–	–	1.4	–	–
Lethane® 384	4.0	1.8	450	1.5	.27	135
Lauryl thiocyanate	19.5	–	–	6.0	–	–
Lethane® 60	32	–	–	8.1	–	–
Pyrethrins	0.045	.02	5	0.047	.085	42
Pyrethrins + 2% IBU*	0.026	.012	3	0.038	.007	3.5
Thanite®	75	–	–	3.2	–	–

(18) Lindane and other compounds vs. Blattella germanica: 356,2357

Insecticide	Lethal Deposit$_{50}$ (μg/cm^2)		
	Insects Sprayed	Insects Dusted	Container Dusted
Lindane	2.8	0.8	0.2
Chlordane	1.7	2.0	0.6
DDT	40.0	15.0	2.5
Sodium fluoride	–	130.0	40.0

(19) Lindane and other compounds as contact insecticides for Periplaneta americana, Blattella germanica; as powders, with insects entering the dust-treated area ad libitum: 2181

Toxicant	LD$_{70}$ (10 days) P. americana		LD$_{70}$ (4 days) B. germanica	
	(μg/insect)	(μg/g)	(μg/insect)	(μg/g)
Lindane	72	69	3.6	31
DDT	37	36	25	217
Pyrethrins*	10.8	10.4	5	43
Sodium fluoride	1833	1763	158	1375

*Yielded highest degree "knockdown" in 1 hour followed in order by lindane, DDT.

(20) Lindane and other substances vs. Cirphis unipuncta (larva) 3268

Toxicant	Topical Application		Oral (On Leaves)		Ratio LD$_{50}$ to LD$_{99}$	
	LD$_{50}$ μg/g	Ratio To Parathion	LD$_{50}$ μg/g	Ratio To Parathion	Topical	Oral
Lindane	28.1	7.6	27.9	11.2	3.2	5.1
Parathion*	3.7	1.0	2.5	1.0	3.4	8.5
DDT	193.0	52.2	45.7	18.3	4.7	22.8
Chlordane	117.5	31.6	78.2	31.3	4.9	4.7
Toxaphene®	56.2	15.2	34.1	13.6	4.7	2.9
Aldrin	19.8	5.4	11.4	4.6	3.7	24.7
Dilan®	8.8	2.4	11.5	4.6	5.4	5.0
Dieldrin	8.3	2.2	4.6	1.8	3.1	3.8

*Parathion yielded the most rapid kills followed in order by Dilan®, lindane, DDT.

e) Effects of lindane on beneficial insects:

(1) Toxicity for honeybee, Apis mellifera, of Lindane and other compounds: (Also consult the section in this work titled, Bees and Insecticides.) 1718

Insecticide	Oral Dosage To Give 24 Hr. Kills Of			Contact Spray To Give Kills Of			Residual Films μg/cm^2 Giving 100% Kills In 24 Hrs. After 1 Hr. Exposures
	20%	50% μg/bee	90%	20%	50% μg/cm^2	90%	
Lindane	.026	.079	.346	.77	.85	.986	.44
Parathion	.018	.04	.144	.257	.354	.574	5.0
TEPP	.052	.065	.093	.358	.445	.621	At 5.5-0% kill
Dieldrin	.223	.269	.354	.386	.575	1.05	.28
Aldrin	.181	.239	.365	.327	.562	1.27	.74
Chlordane	.831	1.12	1.73	3.80	5.0	7.58	3.7
Systox®	1.25	1.48	1.88	4.32	5.12	6.62	At 18.5-0% kill
Dimefox	1.25	1.90	3.51	16.52	23.17	38.64	At 74.0-0% kill
Toxaphene®	25.12	39.81	80.17	36.73	44.67	59.98	70.0

Mortality of Apis mellifera, in contact for 1 hr. with various residual films:

Insecticide	Dry Film (μg/cm^2)	% Kill 24 Hrs.	Average Field Dose (μg/cm^2)	Ounces/ acre
Lindane	0.28	100	2.8	4
"	0.074	0		

Mortality of Apis mellifera, in contact for 1 hr. with various residual films:

Insecticide	Dry Film ($\mu g/cm^2$)	% Kill 24 Hrs.	Average Field Dose ($\mu g/cm^2$)	Ounces/ acre
Dieldrin	0.09	90	1.4	2
"	0.04	10		
Aldrin	0.09	75	1.4	2
"	0.04	0		
Parathion	0.54	90	1.4	2
"	0.18	10		
Chlordane	3.4	100	11.2	16
"	0.9	12		
Systox®	10.0	50	—	—
"	6.8	22		
TEPP	0.22	8	5.6	8
Toxaphene®	110.0	9	16.8	24
"	40.0	0		
Dimefox	50.0	0	—	—

(2) Considered hazardous and unsafe for honeybees when used on bee-frequented plants in bloom. 3099

f) Pharmacological, pharmacodynamic, physiological, etc.; insects:

Entrance into insect body: 847,319,114,846

(1) Penetration of insect cuticle rapid; topical and injected dosages rather similar for mortality.

(2) Penetration of the γ-isomer of BHC (lindane) through insect integument more rapid than other isomers. 114

(3) Amounts taken up from deposits in contact with insects are in approximate ratio to solubility of the 114
BHC isomers in hydrocarbon solvents. Solution in waxes of epicuticle deemed first stage of pick-up
by insects in contact with lindane.

(4) Lindane is intrinsically more toxic than the other BHC isomers by reason of its structure. Toxicity 114,2119
of deposits of γ-BHC and δ-BHC on filter paper to Sitophilus granarius in contact with the deposits: 353

Isomer	Exposure Time (Hrs.) To 11 $\mu g/cm^2$ Deposits	% Kill At Stated Hrs. After Removal From Contact			
		0 hrs.	24 hrs.	48 hrs.	72 hrs.
Lindane (γ-isomer)	0.5	0	53	85	94
"	1.0	0	48	90	97
"	4.0	0	92	95	97
"	7.0	50	81	97	—
"	12.0	80	89	—	—
"	22.0	84	96	100	—
δ-BHC	22.0	0	0	0	0

Mode of action in insect body: (also consult BHC and Addendum)

(1) Essentially unknown. Loosely classified as a neurotoxic insecticide. 353,2231,2119

(2) Gross symptoms of intoxication: Blattella germanica (dusted): Showed excitation within a few 353,2744
minutes, paralysis in 20-40 minutes, death in a few hours; Periplaneta americana: Rapid onset
of tremors then ataxia, convulsions, loss equilibrium then paralysis.

(3) Physiological signs: Blattella, sprayed at LD_{50}: Death within 2.5 hr.; O_2 consumption 6 times 1441
normal in convulsive stage, declining to 2 times normal before death; injected with 1 μg: Immediate 2041
rise O_2 consumption (O_2 uptake 5 times normal in 1 hr. [convulsive stage]) then decline of respiratory 2042
rate with onset of paralysis. Similar effects in Oryzaephilus surinamensis. (Indication of relative
degree of excitation or narcosis.)

(4) Spontaneous discharge (crural nerve) in brief bursts at $\frac{1}{2}$ second periods, when lindane was applied 2318
to leg of Periplaneta. 520

(5) Does not stimulate motor nerves of Periplaneta or Calliphora; action on ganglia, and must be mediated 295
by intact reflex arc to yield tremors and convulsions.

(6) Acetylcholine (free) was increased in nerve cord of poisoned Periplaneta. 3096

(7) Lindane had little influence on heart rate of Periplaneta; pulsation irregular at 100 $\mu g/g$, injected. 2421
Transport of lindane is via haemolymph chiefly; also via nerve tracts. 295

(8) Although the action of lindane has been called DDT-like, essential differences have been noted. 422

(9) Vs. Periplaneta, lindane has a rather slight negative temperature coefficient; the LD_{50} at 32°C being 1305
ca. 2 times that at 14.5°C, (in contrast to DDT where the difference is 20 times); vs. Musca lindane 1561
is reported to have shown similar toxicities at 70° and 90°F; the same is true of Melophagus ovinus. 1559

(10) Metabolism of lindane: Lindane-R strains of Musca metabolize lindane more rapidly than susceptible 2415
biotypes; a dose of 0.3 μg/fly was completely metabolized in 24 hrs. by lindane-R biotypes, although 320
the insects died. The metabolite(s) remain unknown. Metabolism of lindane in other insects is 2227
entirely unknown. Inhibition or blockage of meso-inositol by lindane has been advanced as a theory 3087
(vide supra) both with mammals and insects, with the same equivocal results as to confirmation 846
in both cases. Cytochrome oxidase from Periplaneta coxal muscle is completely blocked in vitro 2945
by lindane at 10^{-3} M as measured by O_2 uptake in the Warburg apparatus; there is transient 817,2208
stimulation at 10^{-5} M. 2305

Resistance to lindane by exposure selection:

(1) A stock of Musca domestica bred for 28 generations in a BHC contaminated laboratory yielded but 6% mortality to a lindane dosage giving 40% kill vs. the unselected progenitor of the strain. 259

(2) Resistance "developed," in response to exposure selection of Musca to chemically similar insecticides, revealed a parallel elevation of lindane resistance. Biotypes resistant to unrelated insecticides, e.g. Thanite®, may show relative "vigor tolerance" vis-a-vis lindane. 2098,3320 3321,765 1259

(3) The high lindane resistance of the LDD and Ballard strains has been noted in the table of toxicities, 3.8 and 15 μg/fly as against ca. 0.01 μg/fly for unselected laboratory biotypes. 3320

(4) Parallel rise in lindane resistance with rise in DDT resistance; Musca domestica: 2098

	LD_{50} (μg/fly) For				
	Laboratory	Riverside	Ontario	San José	Bellflower
Lindane	0.01	0.06	0.05	0.05	0.08
DDT	0.02	0.5	0.5	0.7	10.0

(5) Exposure of Drosophila melanogaster and Blattella germanica to lindane selection has revealed no resistant biotypes in terms of increased LD_{50} values; D. melanogaster has shown a marked vigor tolerance to residual deposits of lindane. 1597

(6) More rapid metabolism of lindane in certain resistant Musca biotypes has been noted above.

Synergism:

(1) Lindane has shown a certain synergistic response with some pyrethrin synergizing compounds tested vs. Tribolium castaneum: 1509

Deposit (mg/10 cm²)	% Mortality (6 days) With Direct Sprays Of			
	1% Lindane + 10% Benzene	1% Lindane + 10% Benzene + 5% n-Octyl sulfoxide of isosafrole	1% Lindane	1% Lindane + 5% n-Octyl bicycloheptene dicarboximide
3.0	58	96	46	55
4.5	84	96	74	74
6.75	92	96	84	92

Hazard to Wildlife:

a) Accidental introduction into a stream of a "large" quantity of a mixed lindane formulation killed all fish over a distance of 1 kilometer. 1296

b) 0.05 ppm of lindane in standing water, 10 cm deep, killed 70-80% of a trout "population" in 6 days. 63

(1) If water containing 0.05 ppm lindane begins to flow gently at the end of 1 day, or immediately if it contains 0.15 ppm lindane, there is reported to be no danger to trout. 63

Experiences reported in the control of insects with lindane:

(1) Vs. Melanoplus: In sparse vegetation, effective at 0.25 lb/acre (3-5 lb/acre as dusts). 334,1100

(2) Vs. Chlorochroa uhleri: Highly effective, (DDT ineffective). 353

(3) Vs. Toxophora graminum: 3% dust needed for control; 2% dusts inadequate. 683

(4) Vs. Chorythucha arcuata: Control given by suspensions of. 1781

(5) Vs. Hyalopterus arundinis: Controlled by 0.02% sprays (99% control). 751

(6) Vs. Rhophalosiphum pseudobrassicae: 1% dusts effective. 3281

(7) Vs. Myzus persicae: 1.5% dusts inferior to parathion. 510

(8) Vs. Heliothrips haemorrhoidalis: 10 times as toxic as DDT. 2227

(9) Vs. Agrotis orthogonia: Effective, but less so than others (toxaphene, chlordane, DNOC, pyrethrins). 350

(10) Vs. Pieris rapae and Trichoplusia ni: Gave 84.2% control. 796

(11) Vs. Diaphania nitidalis: Controlled by 0.5% dusts. 69

(12) Vs. Melittia satyriniformis: As a soil treatment, fully effective. 1614

(13) Vs. Cephus cinctus: Susceptible to lindane; resists DDT. 353

(14) Vs. Tipula spp: In sod, controlled by 1.4 lb per acre. 723

(15) Vs. Wireworms: 0.2 lb/acre (in soil controls in tobacco fields; 2-12 oz/acre gave control; successful as seed dressing at 2 oz per bushel of seed (cereals) optimum concentration = 20-30% lindane in a dressing with an organomercurial disinfectant; safe as to germination at these concentrations. 0.5-4 oz per 100 lb seed protected beans, peas, barley, cucumber, tomato, corn, sugar beet, milo. 112,1674 1675 1485

(16) Vs. Ctenicera aeripennis destructor: 0.5-1.0 lb/acre controlled. 121

(17) Vs. Melanotus and Conodermus: 0.2% dusts controlled in sugar cane. 435

(18) Vs. Limonius canus: Effective as seed dressing. 1912

(19) Vs. Anomala orientalis: 7.5 lbs/acre in soil gave complete control. 2726

(20) Vs. Diabrotica duodecempunctata: 0.2 lb/acre on soil before planting controlled. 1876

(21) Vs. Diabrotica longicornis and D. virgifera: 1 lb/acre in soil greatly reduced. 1530

(22) Vs. Anthonomus grandis: 0.3 lb/acre effective. 91

(23) Vs. Conotrachelus nenuphar: 0.1% spray gave 60% kills of soil form. 2859

(24) Vs. Chorioptes bovis (mange on horses): Dips at 0.015% proved curative. 2980

(25) Vs. Acomatocarus australiensis: 1.5 lb/acre gave 95-99% control. 2163

(26) Vs. Damalinia bovis and D. canis: 0.02%-dips, 0.005% sprays, 0.0025% emulsion controlled. 2980,1084

(27) Vs. Haematopinus spp.: 0.1% emulsion controlled; eggs also killed. 3275

(28) Vs. Haematopinus adventicius: 1% dusts controlled. 3066
(29) Vs. Solenoptes capillatus: 0.04% dips controlled. 1084
(30) Vs. Phormia regina and Lucilia serricata (wool maggots): 0.1% sprays gave 95% control. 3066
(31) Vs. Melophagus ovinus: 0.1% emulsions gave ca. complete control. 3066
(32) Vs. Sitophilus oryzae and Rhizopertha dominica: 0.4 ppm in top 6 inches of wheat piles effective (however there was tainting). 1129
(33) Vs. European Corn Borer (larvae): 0.125 lbs per 100 gal spray gave 92.5% kills. 1343
(34) Vs. Tribolium confusum: Exposure to residues at 1 mg/36 in^2 for 24 hrs. gave 100% kills. 1343
(35) Vs. Aëdes taeniorrhynchus: 0.05-0.1 lb/acre gave good control of DDT resistant type. 1802

Addendum; Recent data on the metabolism of Lindane in insects:

1) Both Lindane non-R and Lindane-R biotypes of Musca domestica metabolize uptaken lindane. 2977
   a) Lindane-R biotypes metabolize the toxicant at an accelerated rate.
   b) Absorption, following topical application of lindane, is ca. the same in both R and non-R biotypes.
   c) DDT- dehydrochlorinase is not involved in the metabolism.
   d) Pentachlorocyclohexene appears to be intermediate in the metabolic degradation of lindane. 0.5 to 2 hours after lindane treatment recovery of the theoretical quantity may be accounted for in terms of lindane + pentachlorocyclohexene and other compounds.
      (1) Since, later than this period (0.5-2 hours), pentachlorocyclohexene does not increase, even though lindane continues to decrease, pentachlorocyclohexene is assumed to be a metabolic intermediate.
      (2) Both Lindane-R and Lindane-non R biotypes readily metabolize pentachlorocyclohexene to other products.
      (3) Relatively large amounts of lindane-free pentachlorocyclohexene are obtainable from Musca exposed for 4 days in heavily lindane-coated cages, then transferred and held for one day in lindane-free (clean) cages.

115

LONCHOCARPUS (=Robinia.)

A genus of leguminous trees or shrubs e.g. L. utilis, L. urucu, L. hicou used insecticidally in the form of the dry, powdered roots, or extracts of these roots. The active principle is Rotenone, q.v., (also see Derris), usually present in amounts of 8-11% with lesser quantities of related compounds. The genus is native to Central and South America, and the dried product in commerce is referred to as "Timbo" or "Cubé." The maximum rotenone content of such products is ca. 20%, with the average as already stated. 1866

116

MAGNESIUM ARSENATE (Trimagnesium orthoarsenate)

$Mg_3(AsO_4)_2$ Molecular weight 330.78

GENERAL [Refs.: 1613,1006,1025,586,577,325]

The commercial product is a mixture of the dimagnesium salt, $MgHAsO_4$, and 2 basic salts $Mg_3(AsO_4)_2 \cdot MgO \cdot H_2O$ with the basic salts predominating. Commercial brands yield an As_2O_5 content of 31.8%-32.69%. Resembles the calcium arsenates in many properties. Has been used for control of Epilachna varivestis under conditions in which calcium arsenate has proved inadequate and has given excellent results without plant injury. The compound is soluble in the intestinal secretions of Epilachna, the pH being acid; almost lacking in toxicity for Bombyx mori whose gut secretions are alkaline (pH 8-9) and, being insoluble under alkaline conditions, is excreted unchanged. Effective against Popillia japonica in soil when first applied, but is soon decomposed and harmless.

PHYSICAL, CHEMICAL

A white crystalline powder, $Mg_3(AsO_4)_2 \cdot H_2O$ in long, needle-like crystals or short flat prisms, $Mg_3(AsO_4)_2 \cdot 2H_2O$ in very small, lenticular crystals; odor: None; taste: Salty; virtually insoluble in water.

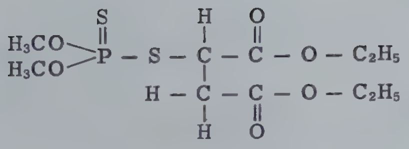
TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Poisonous. No quantitative data available to this compilation.

2) Toxicity for insects:
   a) Consult in this work the section titled, Arsenic and Arsenicals.

117

MALATHION [Malathon, formerly] (O,O-Dimethyl S-(1,2-dicarboethoxyethyl) dithiophosphate; S-(1, 2-Dicarbethoxyethyl) O,O-dimethyl phosphorodithioate; S-(1, 2-Dicarbethoxyethyl) O,O-dimethyl dithiophosphate; S-1:2-bis-(Ethoxycarbonyl) ethyl-O,O-dimethyl thiophosphate; O,O-Dimethyl thiophosphate of Diethyl mercaptosuccinate; Experimental Insecticide 4049 [American Cyanamid Co.].)



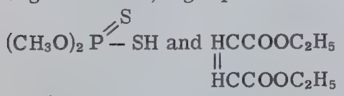
Molecular weight 330

GENERAL [Refs.: 2802,1801,2231,353,1092,1308,1458,1123,854,3188,1085,2582,1915,2862,473,775]

A member of the general class known as organic phosphate or "organophosphorus" insecticides. Combines a relatively low mammalian toxicity with an exceptionally wide range of activity against phytophagous mites, mammalian and avian lice, aphids, scale insects, flies and several score insects, both sucking and chewing, of fruits, vegetables and ornamental plants. At present, one of the few organic phosphate insecticides considered safe enough to justify availability in commerce for general insect control use. Toxic to insects by contact, ingestion, and possibly by short range "fumigant" action. Penetrates and traverses plant tissue, e.g. from one face of leaf to the other; aphids on undersurface killed by applications on upper surface of leaf; 100% kill is given in such circumstances by twice the direct contact dose.

PHYSICAL, CHEMICAL [Refs.: 2231,353,2802,775,1554]

Pure: A yellowish oily liquid; technical (the compound available in commerce): A dark brown liquid having a strong smell of garlic; the technical grade is 95-98% pure in terms of the substance whose formula appears above; m.p. 2.85°C (99% pure); b.p. 156°-157°C (with slight decomposition at the b.p.) $d_{4°}^{25°}$ (technical) 1.23; $n_D^{25°}$ (99% pure) 1.495; v.p. 4×10^{-5} mmHg at 30°C; slightly soluble in water (to 145 ppm); miscible in most commonly employed organic solvents; limited solubility in petroleum oils; hydrolysis rapid at pH >7 and <5; stable in buffered (pH 5.26) aqueous solution; incompatible with alkaline spray materials, for example, Bordeaux mixture; compatible with most commonly used non-alkaline materials, for example, DDT, lead arsenate, methoxychlor, mineral oil, parathion, DDD, ferbam, glyodin, captan, tribasic copper sulfate, sulfur, zineb, ziram; with alkaline materials, initial kills by malathion are not significantly decreased, but residual toxicity suffers; common solvents for include: Alcohols, esters, ketones, ethers, aromatics, alkylated aromatic hydrocarbons, vegetable oils; light petroleum oil (30°-60°C) is soluble in malathion to 35%. Prepared by the interaction of



$$(CH_3O)_2\overset{S}{\overset{/\!/}{P}}-SH \text{ and } \begin{array}{c}HCCOOC_2H_5\\ \|\\ HCCOOC_2H_5\end{array}$$

- a) Formulations: Emulsifiable concentrates employed at 125 to 250 cc per 100 l or 1 to 2 pints per 100 gallons water; wettable powders (25%) used at 240 g per 100 l or 2 lbs per 100 gallons; dusts (4%) used at 32 k per hectare or 30 lbs per acre.
- b) Residues:
  - (1) Disappear rapidly; wash off readily. Time interval between last application and harvest = 7 days (on some crops 72 hours). 2386
  - (2) Residue tolerance (Miller amendment to Public Law 518) is 8 ppm actual malathion in or on raw agricultural commodities.
- c) Certain precautions:
  - (1) Not to be used in dwellings. Not to be applied to freshly white-washed surfaces until 14 days have passed.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
- a) Ca. 100 times less toxic than parathion, q.v., for mammals (and $\frac{1}{4}$ to $\frac{1}{3}$ as insecticidal). $\frac{1}{4}$th as toxic, orally (mouse,) as the diethyl ester (but for insects relatively more toxic). 1709 1458
- b) Esters of dithiophosphoric acid present an unusual range of toxic structure. 1656
  - (1) Some, for instance, O,O-diethyl (S-2-ethyl mercapto methyl)-[and -S-2 isopropyl mercaptomethyl-] dithiophosphates, are more toxic than parathion for mammals by 5 to 10 times.
  - (2) Some possess not only high contact activity vs. insects, but systemic insecticidal activity in the tissues and sap-stream of plants.
  - (3) Malathion excels in low relative toxicity for mammals, for example, <0.001 the toxicity of the -S-2-ethyl mercaptomethyl- compound above. 1656
  - (4) The reduced mammalian toxicity may be due in part to poor absorption into the blood stream and nerve tissue via the oral route. 2231

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse (♂)	or	LD_{50}	885	Tech. 90%; given in corn oil..	1577
Mouse	or	LD_{50}	1120		1331
Mouse	or	LD_{50}	930 (♂); 940 (♀)	Tech. 65%; given in propylene glycol.	1216
Mouse	or	LD_{50}	720 (♂)	Tech. 90%; " vegetable oil.	1216
Mouse	or	LD_{50}	3300 (♂)	Tech. 99 + %; given undiluted.	1216
Mouse	or	LD_{50}	2700 (♂)	" " in vegetable oil.	1216
Rat	or	LD_{50}	300 (♂); 600 (♀)	Tech. 65%; given in propylene glycol.	1216
Rat	or	LD_{50}	940 (♂)	" 90%; "	1216
Rat	or	LD_{50}	390 (♂)	" " " vegetable oil.	1216
Rat	or	LD_{50}	4700 (♂)	" 99 + %; given undiluted.	1216
Rat	or	LD_{50}	1500 (♂)	" " " in vegetable oil.	1216,1331
Rat	or	LD_{50}	1200 (♀)		1331
Rat	or	LD_{50}	480 (♂)	" 90%; given in corn oil.	1577
Rat	or	LD_{50}	1156 (♂)		1461
Rat	or	LD_{50}	1400 (♀)		854
Rat	or	LD_{50}	2100 (♂)	" 95%; given undiluted.	1216
Rat	ct	LD_{50}	> 4000	In single acute exposure.	2231
Rat	ip	LD_{50}	750 (♀♂)		854
Rat	iv	LD_{50}	ca. 50		1331
Guinea Pig	or	LD_{50}	570		1331
Calf (<3 wk of age)	or	LD_{50}	80	Given undiluted as tech. 95%.	1216
Cow	or	LD_{50}	560 (♀)	" " " " "	1216
Rat	or	LD_{50}	1156		1461

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Chicken (New Hampshire)	or	LD_{50}	>850	Tech. 95% given in vegetable oil.	1216
Calf (baby)	or	MTD*	20	*=Minimum Toxic Dose.	2567
Sheep	or	MTD*	100	*= " .	2567

c) Experiences with single acute inhalation of vapors; rats and mice:
   (1) At 30°C, air saturated with malathion contains ca. 0.5 ppm. 1216
   (2) In air saturated via a bubbler, held at 100°C in a bath, rats (7) and mice (13) exposed 8 hrs: 1 mouse dead during exposure; others: Full recovery, in 30 minutes after end of exposure, from symptoms which included: Excessive preening, depression, labored respiration; no evidence of irritation. Heating of air stream may have affected toxicity. 1216

d) Repeated exposure to aerosols: At 60 ppm; rats: No toxicity save local irritation; no effect on choline esterase activity. At 5 ppm, exposure >4 weeks yielded no overt toxic signs; at autopsy, slight lung irritation noted. 1458

e) Single applications to eye:
   (1) $\frac{1}{20}$ cc undiluted 95% tech. in conjunctival sac, rabbits: Gave slight immediate irritation (mild conjunctivitis, slight lid oedema, injection of sclera) subsiding in 24 hrs; no signs of systemic intoxication. 1216

2) Subacute toxicity; higher animals: (Also consult Addenda)

a) Repeated dermal application: 1216
   (1) Chickens: 4% dusts applied once a week for 6 weeks at ca. 0.4 mg/cm^2 body surface/wk: No deaths; no overt toxic signs; no significant lowering of plasma, brain, liver, ileum choline esterase activity during treatment or at 1 week after end of treatment.
   (2) Chickens: Emulsions 95% technical at 7 mg/cc applied once a week for 6 weeks, massaged into feathers and skin to run-off at ca. .03 cc/cm^2/week or 0.2 mg/cm^2/week 95% tech. malathion: No deaths, no overt toxicity, no diminution in choline esterase activity.
   (3) Cattle: Emulsion spray at 7 mg/cc (approx.) 95% tech. malathion, once a week 6 applications to adults and calves; application at .03 cc/cm^2/week (cows) 0.06 cc/cm^2/week (calves) or 0.2 mg/cm^2/week and 0.4 mg/cm^2/week respectively: No overt toxic signs; no significant evidence of choline esterase inhibition.
   (4) Cattle: Emulsion and suspension sprays 95% tech. malathion at 0.5% strength in 95% tech. malathion once a week; 16 applications: No overt toxic signs; depression of choline esterase activity during treatment, recovery partial to complete in 3 months post-treatment. Cattle, receiving 2 sprayings to run-off of 1% and 0.5% emulsion spray and suspension spray respectively: No diminution of choline esterase activity.
   (5) Goats: Dipped in 0.25% emulsion and 0.1% suspensions (animals sheared before treatment) one time: No effect on choline esterase activity.
   (6) 2460-6150 mg/k required for single application toxicity in rabbits; ca. 1230 mg/k (90% tech.) = MLD, dermal for Guinea pigs. 129
   (7) Pigs sprayed at rate of 1 qt. each with 0.5, 1.0, 2.0% malathion prepared from emulsifiable concentrate showed no signs of toxicity or irritation during the 2 weeks post-treatment. 1747

b) Repeated vapor inhalation: 1216
   (1) Rats and mice exposed twice (2 hrs. 45 min. exposure 1st day, 7.5 hr. exposure 2nd day:) in air near-saturated with 99% malathion (tech.): 1 of 13 mice died, 0 of 7 rats died; all showed signs of discomfort; prompt recovery of survivors.

c) Repeated feeding (33 days exposure) of 95% tech. malathion in the diet; rats: 1216

Concentration (ppm):	0.0	100	100	5000
Number of animals:	10	10	10	10
Mean dosage, mg/k/day:	—	10	90	470
Mean food intake, g/rat/day:	14.7	16.5*	16.0*	15.4
Mean wgt gain g/rat	127	154*	147*	124

Choline esterase activity as mean % of activity in controls

Number of animals:	10	6	6	6
Plasma ChE:	—	94	94	78*
Erythrocyte ChE:	—	93	68*	22*
Brain ChE:	—	98	96	100
Liver ChE:	—	100	95	73
Deaths:	0	0	0	0

*Value significantly different (p=.05) from control.

   (1) Chickens: Entire group of subjects on 10 ppm 95% tech. malathion for 2 weeks then divided into groups receiving 100, 1000, 5000 ppm for 10 wks: No deaths at 100 ppm, 1000 ppm; some plasma ChE inhibition at 1000 ppm; appearance and behavior normal; at 5000 ppm: Distinct toxic signs (growth retard, slow feather growth, soft feces, leg weakness, paralysis); 2 of 10 dead in 2nd week, 1 in 5th week, 1 in 6th week; at autopsy: No pathological signs; ChE activity significantly inhibited (plasma) in survivors at 6, 8 weeks and plasma and brain ChE at end of 10 weeks. Mean daily dosage at 100 ppm = 7 mg/k, at 1000 ppm = 90 mg/k at 5000 ppm = 450 mg/k. 1216

3) Chronic toxicity; 2 year feeding experiences; rats: 1216, 1461

a) 90% tech. malathion as 25% wettable powder:

ppm*		mg/k/day (Mean)	No. Survivors/ No. Tested	Effect On Food Intake	Effect On Growth	Degree ChE Inhibition At Post-Mortem		
						Plasma	Erythrocyte	Brain
100	(♂♂)—	6	15/20	0	0	Slight	Slight	Slight
1,000	(♂♂)—	60	11/20	0	0	"	Marked	"
	(♀♀)—	80	8/10	0	0	0	"	"
5,000	(♂♂)—	350	14/20	0	Retard	Marked	Complete	Marked

99 + % tech. malathion as 25% wettable powder:

ppm*		mg/k/day (Mean)	No. Survivors/ No. Tested	Effect On Food Intake	Effect On Growth	Plasma	Erythrocyte	Brain
500	(♂♂)—	30	2/4	0	0	0	Marked	0
	(♀♀)—	40	3/4	—	—	0	"	0
1,000	(♂♂)—	60	2/4	0	0	0	Marked	Slight
	(♀♀)—	80	1/4	0	0	0	Complete	Slight
5,000	(♂♂)—	380	3/3	Reduced	Retard	Slight	"	Moderate
	(♀♀)—	380	3/4	"	0	"	"	Slight
20,000	(♂♂)—	720	0/3	All ♂♂ died within 20 days				
	(♀♀)—	1800	2/3	Reduced	Retard	Marked	Complete	Marked

*In terms of malathion technical of the stated grade of purity.

Controls		
	(♂♂)	10/20
	(♀♀)	5/10

(1) Tolerance of rats for malathion in diet is relatively great (for an organic phosphate insecticide).
(2) Symptoms (overt) few or none.
(3) To 5000 ppm slight effect on survival, food intake, growth; some males have survived 10,000 ppm for 1 yr., some ♂♂ have survived 20,000 ppm for 2 years, with serious effects on growth, food intake, general health.
(4) Gross and microscopic examinations for pathological signs revealed no structural changes in organs or tissues attributable to malathion.
(5) Effects on ChE activity are evident from table (supra).

4) Pharmacological, pharmacodynamical, physiological, etc.: (Also consult the general treatment in this work titled, Organic Phosphates).

a) The pharmacological action of malathion is mediated by the inhibition of tissue choline esterase and the ensuing overt signs of toxicity, after large single doses in experimental animals, are almost exclusively characteristic of cholinergic intoxication. 1216

(1) Among the symptoms in small experimental animals the predominant signs are. Excess salivation, depression, tremors.
(2) In case of lethal doses the symptoms given are succeeded by coma and death.
(3) The less serious symptoms in case of non-fatal intoxication are of short duration; unless death occurs within several hours recovery is rapid and complete.
(4) The regeneration of choline esterase to full normal levels may require considerable time even after the disappearance of overt symptoms.

b) ID_{50} for rat serum choline esterase in vitro = 8×10^{-3} M; for rat erythrocyte ChE = 2×10^{-5} M. 1458, 854

c) ID_{50} for choline esterase inhibition in vivo = 1×10^{-1} M; this is associated with an intraperitoneal LD_{50} (rat) of 750 mg/k and may be compared with some other organic phosphates of the alkyl phosphorothionate category as follows: 713, 861

Compound	LD_{50} (ip, rat) mg/k	ID_{50} (in vivo)
Malathion (90% tech.)	750	1×10^{-1} M
Parathion	5.5	1.2×10^{-6} M
Metacide	3.5	1×10^{-9} M
Potasan®	15.0	5×10^{-5} M
Systox®	3.0	5×10^{-7} M

d) The inhibition of choline esterase by malathion is to a degree greatly less than in the case of other organic phosphate insecticides. 1216

e) Comparison of the anticholine esterase activity of Malathion and Parathion: 1709

Insecticide	ID_{50} Brain ChE in vitro Molar Conc. x 10^{-6}			Ratio ID_{50}		Anti-ChE Rating			LD_{50}, Oral ♂ Mouse	
	Bee	Fly	Mouse	Mouse/ Bee	Mouse/ Fly	Bee	Fly	Mouse	mg/k	M x 10^{-5}/k
Malathion	15	0.95	150	10	42.8	6.67	128.6	1.67	930	282
Parathion	1	0.45	2.5	2.5	5.5	← 100 (arbitrary) →			9.7	3.3

f) Metabolic fate of P^{32} labelled malathion in hen and mouse: 2092

(1) 60% of malathion consumed orally by hens was eliminated in feces in 2-4 days; 75% in 5-6 days.
(2) 97% of the excreted radioactivity was in form of water soluble metabolites, degradation products.
(3) Maximum amount in tissues was <3% of amount fed.

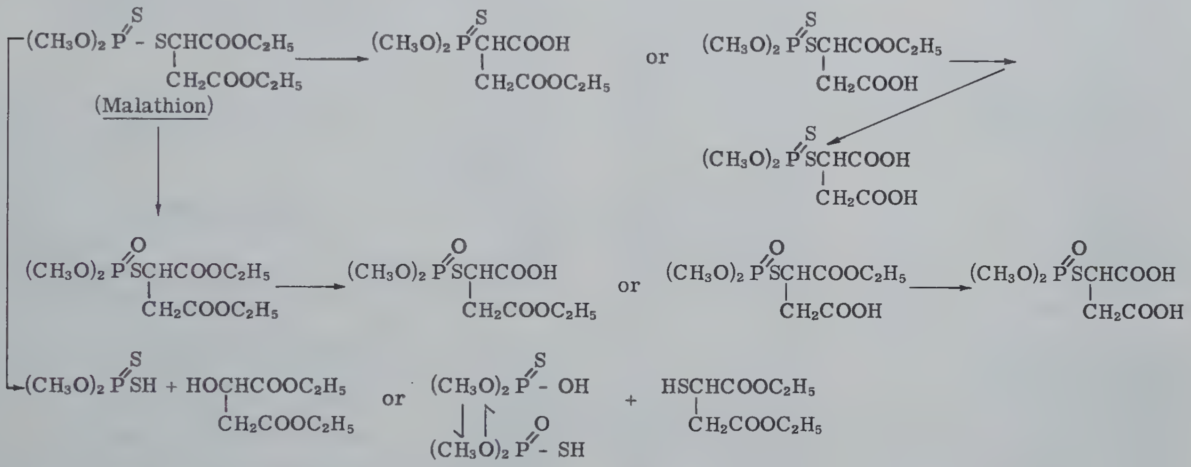
(4) In sprayed hens the largest concentration of radioactivity appeared in feces 24 hrs. post-treatment, and was ca. 50% that of fed hens at maximum; less than 12% of applied malathion was absorbed and eliminated in 32 days; skin absorption was poor, and malathion was unavailable for absorption from the feathers; 90% of excreted radioactivity was as water-soluble metabolites and degradation products; residues in tissues and eggs = ca. $\frac{1}{10}$th the amount found in hens after oral dosage with malathion.

(5) Massive intraperitoneal doses in hens: >50% eliminated in 3 hours; ca. 100% eliminated in 24 hrs.; at period of maximum elimination (1-3 hrs. after injection) ca. twice as much radioactivity was eliminated as unchanged malathion and as chloroform-soluble metabolites than was eliminated as water-soluble metabolites or degradation products; at other times, 90% of excreted radioactivity was in form of water-soluble metabolites and degradation products.

(6) No gross toxic effects in hens fed at 100.6 ppm or sprayed with 0.5% w/w malathion spray at 38 cc/bird (♂); 0.16-0.25 cc/bird of malathion is apparently tolerated.

(7) The metabolism of malathion in the chicken is potentially complex; postulated is a progressive hydrolysis of ethyl ester moieties to give more ionic and water-soluble compounds with low toxicity; also there is oxidation of the thiono-sulfur moiety to a series of thiol phosphates one of which (O,O-dimethyl S-(1,2-dicarbethoxy) ethyl phosphorothiolate) may be the principal metabolite, showing marked anti-choline esterase activity and consequent toxicity.

(8) The following metabolic schema is put forward as a possibility:



(9) The metabolism proposed for insects (Periplaneta americana) is identical, vide infra.

5) Hazard for Man:

a) Observation of 12 spray men, handling malathion, for evidences of choline esterase inhibition (plasma, erythrocyte ChE):

(1) 10 using malathion as emulsifiable concentrate (50%) applied on average at 1 pint/100 gal. water; one using malathion at 1 gal. concentrate/150 gal. water; one using malathion as 25% wettable powder at 11 lb/600 gal. water.

(2) In 8 subjects exposures of 8-9 hrs/day for 2-9 days before testing and in the other 4 subjects from 6 hrs/day for 2 days to 6 hrs/day for 13 days.

(3) One subject out of 12 only, taking personal protective measures against exposure.

(4) Result: No instance of depressed choline esterase activity either in plasma or erythrocytes of the foregoing subjects.

6) Phytotoxicity: (Malathion [like parathion] penetrates and traverses plant tissue, for instance, from one face of a leaf to the other).

a) No evidence of phytotoxicity at insecticidal or acaricidal levels reported save for slight damage (glass house conditions) to string beans, squash, cucumber. No phytoxicity on beans (Refugee #5; pot culture) at 1%, 2%, 4% solutions. 2120 775

b) Phytotoxicity reported for Poinsettia at mealy bug control concentrations; unsafe on these plants, save in dormancy. 1451

c) Used, in extreme application, as mist concentrate formulation, on both leaf surfaces to dripping, in an evaluation of relative toxicity for various insecticides and acaricides, malathion yielded damage varying from moderate to kill on the following plants: Cornus amomum, Cotinus coggygria, Viburnum dilatatum, Oxydendrum arboreum, Deutzia scabra, Acer saccharum, Ligustrum obtusifolium Lonicara sp., Sorbaria sorbifolia, Eunonymus bungeanus, Aesculus parviflora, Hydrangea sp., Cladastris lutea, Syringa sp. Average toxicity of 3% solutions of malathion = 7.1 (on a scale where 0 = no injury, 1 = slight injury, 4 = moderate injury, 8 = severe injury, 10 = kill); an average toxicity of 7.7 (on the foregoing scale) was recorded using 5% solutions on the following plants: Ulmus americana, Acer saccharum, Crataegus cordata, Pinus strobus, Populus sp., Salix sp., Quercus palustris, Carya ovata, Viburnum lantana. 553

(1) Average phytotoxicity of malathion under the extreme conditions of test was greater than that of toxaphene, isodrin, endrin, aldrin, dieldrin, DDT, methoxychlor, chlordane, heptachlor, lindane, Ovotran®, Aramite®.

d) Tainting hazard; plant products: 1389

(1) For a non-professional tasting panel the usual dosages of malathion had no adverse effect on the flavor of fresh apples, canned applesauce, canned peaches, canned pears, frozen strawberries, fresh cherries, cooked fresh potatoes, canned wax beans, canned snapbeans, peas.

e) Soil accumulation of malathion is not a problem. According to some it should not be applied to food crops later than 21 days before harvest, save in the case of tomatoes and beans, (10 days) peas and potatoes (14 days). 129

f) Application rate ranges from 0.05 to 0.5 lb/acre. 129

g) The manufacturer (American Cyanamid Co.) warns that hazard of injury may attend use on: McIntosh and Cortland apples (summer sprays); Bosc pears; certain sweet cherry varieties (especially in Northwest); Ribier grapes; on cucurbits unless plants are dry; some ferns; some species of Crassula. 2802

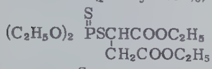
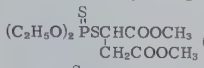
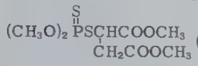
7) Toxicity for insects and acarines:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aëdes nigromaculis (4th instar)	Medium	LC$_{50}$ 24 hr.	0.025 ppm	DDT-R biotypes.	1193
Anopheles quadrimaculatus (adult)♂	Topical	LD$_{50}$	0.0087 μg/insect	Rel. effectiveness (DDT=1) = 2.3.	2051
A. quadrimaculatus (adult)♀	Topical	LD$_{50}$	0.0095 μg/insect	" " = 7.0.	2051
A. quadrimaculatus (adult)♂	Topical	LD$_{90}$	0.019 μg/insect	" " = 2.4.	2051
A. quadrimaculatus (adult)♀	Topical	LD$_{90}$	0.022 μg/insect	" " = 5.9.	2051
Chaitophorus populi	Contact Spray	LC$_{50}$	0.022 g/l	In white spirit; dusting tower application.	775
Chrysops discalis (adult)	Topical	LD$_{50}$ (est)	130 μg/fly		2707
Chrysops discalis (")	Topical	LD$_{90}$	330 μg/fly		2707
Culex tarsalis (4th instar larva)	Medium	LC$_{50}$ 24 hr.	0.0185 ppm	DDT-R biotypes.	1193
Ephestia kühniella (larva, 1 cm.)	Contact Spray	LC$_{50}$	4 g/l	In white spirit; dusting tower application.	775
Fannia canicularis (adult)♀	Topical	LD$_{50}$ 24 hr.	0.10 μg/fly	In acetone; measured drop method; av. wgt. 6.89mg.	1981
Fannia canicularis (")♂	Topical	LD$_{50}$ 24 hr.	0.06 μg/fly	" " " 7.35mg.	1981
Heliothrips haemorrhoidalis	Contact Spray	LC$_{50}$	0.00016% w/v		2092
Mosquito (larva)	Medium	LC$_{80}$	$<$0.00001% w/v		2092
Musca domestica (adult)	Topical	LD$_{50}$	28 μg/g		2231
Musca domestica (")♀	Topical	LD$_{50}$ 24 hr.	0.56 μg/fly	In acetone; measured drop method.	1981
Musca domestica (")	Contact Spray	LC$_{50}$ 24 hr.	0.48 mg/cc	KD 10 min. at LC$_{50}$ = O.	2033
Musca domestica (")	Topical	LC$_{50}$ 24 hr.	27 μg/g		2247
Musca domestica (")	Topical	LD$_{50}$	0.6 μg/fly		2092
Musca domestica (")	Contact Spray	LC$_{50}$	0.74 g/l	In white spirit; dusting tower application.	775
Anopheles quadrimaculatus (larva 4th instar)	Medium	LC 48 hr.	0.1 ppm	100% kill at this dosage; 96% kill at 0.025 ppm.	1766 2020
Myzus persicae	Contact Spray	LC$_{50}$	0.03;0.098 g/l	In white spirit; dusting tower application.	775
Pediculus humanus corporis	Residue	KD$_{100}$ Time	1 hr.	100% effective for 31 + days.	2020
Periplaneta americana	Injection	LD$_{50}$	8.4 μg/g	Iso-malathion LD$_{50}$ = 60 μg/g.	2391
Protoparce sexta (5th instar)	Topical	LD$_{50}$	481 μg/larva	Large larvae, av. wgt. 5.4(4.1-7.5)g.	1306
Protoparce sexta (")	Topical	LD$_{90}$	1276 μg/larva	" " .	1306
Protoparce sexta (3rd, 4th instar)	Topical	LD$_{50}$	61 μg/larva	Medium larvae, av. wgt. 2.5(1.2-4.0)g.	1306
Protoparce sexta (")	Topical	LD$_{90}$	553 μg/larva	" " .	1306
Protoparce sexta (2nd, 3rd instar)	Topical	LD$_{50}$	23.6 μg/larva	Small larvae, av. wgt. 0.9(0.6-1.1)g.	1306
Protoparce sexta (")	Topical	LD$_{90}$	92 μg/larva	" " .	1306
Protoparce sexta (5th instar)	or	LD$_{50}$	365 μg/larva	Large larvae, av. wgt. 5.4(4.1-7.5)g.	1306
Protoparce sexta (")	or	LD$_{90}$	1621 μg/larva	" " .	1306
Sitophilus granarius (adult)	Contact Spray	LC$_{50}$	0.088;0.092 g/l	In white spirit; dusting tower application.	775
Tenebrio molitor (larva 2-2.5 cm)	Contact Spray	LC$_{50}$	$>$1.6 g/l	" " .	775
Tribolium confusum (adult)	Contact Spray	LC$_{50}$	0.42;0.53 g/l	" " .	775
Paratetranychus citri	Contact Spray	LC$_{50}$	0.0042% w/v		2092
Tetranychus bimaculatus	Contact Spray	LC$_{50}$	0.049 g/l		775
Tetranychus bimaculatus (adult)	Residue	LC$_{50}$ 48 hr.	0.0025 g/100 cc	Emulsifiable conc.;[mites placed on leaves treated in settling tower].	905
T. bimaculatus (larva)	Residue	LC$_{50}$ 48 hr.	0.0073 g/100 cc	" ;["].	905
T. bimaculatus (egg)	Residue	LC$_{50}$ 48 hr.	0.32 g/100 cc	" ;["].	905
T. bimaculatus (adult)		LC$_{50}$ 48 hr.	0.084 g/100 cc	" ;[mites placed on leaf surface opposite treated surface].	905
T. bimaculatus (adult)	Residue	LC$_{50}$ 48 hr.	0.0042 g/100 cc	Wettable powder;[mites placed on leaves treated in settling tower].	905
T. bimaculatus (larva)	Residue	LC$_{50}$ 48 hr.	0.0115 g/100 cc	" ;["].	905
T. bimaculatus (egg)	Residue	LC$_{50}$ 48 hr.	0.84 g/100 cc	" ;["].	905
T. bimaculatus (adult)		LC$_{50}$ 48 hr.	0.125 g/100 cc	" ;[mites placed on leaf surface opposite treated surface].	905
Tetranychus bimaculatus (red form)	Dip	LC$_{50}$ 48 hr.	36 ppm	Mites dipped while on red kidney bean leaves.	565
T. bimaculatus (green form)	Dip	LC$_{50}$ 48 hr.	48 ppm	" .	565
T. bimaculatus (red form)	Dip	LC$_{90}$ 48 hr.	96 ppm	" .	565
T. bimaculatus (green form)	Dip	LC$_{90}$ 48 hr.	120 ppm	" .	565

b) Comparative toxicity malathion and other compounds for insects and acarines:

(1) Comparative toxicity of parathion, malathion, and esters related to malathion; an arbitrary value of 100 assigned to parathion; other values = (X) % as toxic as parathion: 1709

Compound	LD$_{50}$ Oral ♂ Mouse mg/k	Aphis rumicis spray (25% w. pwdr.) 48 hr. Kill	Tribolium confusum Contact (25% w. pwdr.) Dust Tower 72 hr. kill	T. confusum Exposure To Residues Of 25% w. pwdr. Suspensions Settling Tower Tests	Blattella germanica Exposed To Dusted Dishes, 25% w. pwdr. at 25 mg/18 cm diam. dish. Dust Chamber tests	Oncopeltus fasciatus Dust Chamber Tests
Malathion (purity 73%)	930	25	25	24	7	74
Parathion (purity 97.5%)	9.7	100	100	100	100	100
 $(C_2H_5O)_2\overset{S}{\overset{\|}{P}}S\underset{CH_2COOC_2H_5}{\underset{\|}{C}}HCOOC_2H_5$ (purity >70%)	250	11	6	—	10	76
 $(C_2H_5O)_2\overset{S}{\overset{\|}{P}}S\underset{CH_2COOCH_3}{\underset{\|}{C}}HCOOCH_3$ (purity >70%)	48	45	28	29	17	65
 $(CH_3O)_2\overset{S}{\overset{\|}{P}}S\underset{CH_2COOCH_3}{\underset{\|}{C}}HCOOCH_3$ (purity >70%)	130	25	32	34	5	6

(2) Comparative toxicity malathion and parathion, for several insects; toxicants as emulsion concentrates in white spirit; contact spray application by dusting tower method: 775

Insect	Parathion; LC$_{50}$ (g/l)	Malathion; LC$_{50}$ (g/l)	$\left(\frac{\text{Ratio Parathion}}{\text{Malathion x 100}}\right)$
Musca domestica (adult)	0.032	0.74	4.3
Sitophilus granarius (adult)	0.031;0.044	0.088;0.092	45.3;47.8
Tenebrio molitor (larva 2-2.5 cm)	0.165	>1.6	<10
Tribolium confusum (adult)	0.031;0.046	0.42;0.53	7.2; 8.7
Ephestia kühniella (larva, 1 cm)	0.21	>4	< 5
Chaitophorus populi	0.008	0.022	36.4
Myzus persicae	0.0125;0.021	0.03;0.098	21.4;41
Tetranychus bimaculatus	0.02	0.049	41

Persistence of Toxic action (residual action)

Malathion
On bean leaves at 0.2% 24 hrs. later: No toxicity for T. bimaculatus.
On bean leaves at 0.4%;0.8% 48 hrs. later: No toxicity for T. bimaculatus.

Parathion
On bean leaves at 0.1% 48 hrs. later: No toxicity for T. bimaculatus.

Malathion
On poplar leaves at 0.4%, 0.8% 96 hrs. later: No toxicity for Chaitophorus populi.
On poplar leaves at 0.2% 48 hrs. later: No toxicity for Chaitophorus populi.
" at 0.1% 24 hrs. later: " .

Parathion
On poplar leaves at 0.1% 96 hrs. later: " .
" at 0.05% 48 hrs. later: " .
" at 0.025% 24 hrs. later: " .

Malathion
50% kill of Sitophilus granarius given at 6 days after application on filter paper, treated at 0.092% concentration; 50% kills (20 days after application) given by deposits on filter paper of a 0.76% concentration.

Parathion
50% kill of Sitophilus granarius given at 6 days after application on filter paper treated at 0.04% concentration; 50% kills (20 days after application) by deposits on filter paper of a 0.065% concentration.

Both malathion and parathion penetrate and traverse plant tissue, for example, from one leaf surface to the other. Aphids on leaf undersurface are killed by applications of malathion to the upper surface; 100% kills were given by 0.4% concentration (twice the direct contact dose).

(3) Toxicity of malathion and other insecticides to various Diptera: Musca domestica, Fannia canicularis Chrysops discalis; (adult insects). 2033,2247 1981,2707,2231

Insecticide	Musca			†Fannia		Chrysops	
				**Topical LD$_{50}$ 24 Hrs. µg/fly		Topical	
	**Topical LD$_{50}$ (µg/fly)	***Contact Spray LC$_{50}$ 24 Hrs. (mg/cc)	KD in 10 min. % At LC$_{50}$ 24 Hrs.	♀	♂	LD$_{50}$ †† (µg/fly)	LD$_{90}$ (µg/fly)
Malathion	0.56;(27µg/g)	0.48	0	0.10	0.06	130	330
Chlorthion®	0.33;(16.5µg/g)	—	—	0.035	0.022	65	420
Diazinon	0.092;(4.6µg/g)	—	—	0.098	0.054	90	360
Dipterex®	—	—	—	—	—	90	910

(3) Toxicity of malathion and other insecticides to various Diptera: Musca domestica, Fannia canicularis, Chrysops discalis; (adult insects). 2033,2247 1981,2707,2231

Insecticide	Musca			†Fannia		Chrysops	
	**Topical LD₅₀ (μg/fly)	***Contact Spray LC₅₀ 24 Hrs. (mg/cc)	KD in 10 min. % At LC₅₀ 24 Hrs.	**Topical LD₅₀ 24 Hrs. μg/fly ♀	♂	Topical LD₅₀†† (μg/fly)	LD₉₀ (μg/fly)
EPN®	2.0μg/g	—	—	—	—	48	120
Isopropyl parathion	4.8μg/g	—	—	—	—	—	—
Methyl parathion	1.3μg/g;1.0μg/g	0.025	0	—	—	—	—
Parathion	1.4μg/g;0.9μg/g	0.02	0	—	—	—	—
TPDP*	15μg/g	0.69	0	—	—	—	—
TEPP	5μg/g	0.069	ca. 70	—	—	—	—
Aldrin	1.7μg/g	0.056	0	—	—	40	170
Chlordane	4.0μg/g	0.25	0	—	—	60	650
DDT	0.033	0.35	0	2.80	1.30	20	250
Dilan	—	0.72	ca. 30	—	—	—	—
Dieldrin	0.031;(1.1,1.5μg/g)	0.017	0	0.003	0.0026	20	950
Endrin	—	—	—	—	—	9	80
Heptachlor	1.7μg/g	0.052	0	—	—	40	200
Isodrin	—	—	—	—	—	60	170
Lindane	0.01	0.046	0	0.76	0.39	4	35
Methoxychlor	0.068	—	—	0.14	0.12	30	90
Q-137	—	—	—	—	—	120	400
Toxaphene®	31.0μg/g	0.68	0	—	—	180	480
Isolan	—	1.15	100	—	—	—	—
Pyrolan	—	5.5	100	—	—	—	—
Allethrin	—	1.5	100	—	—	—	—
Pyrethrins	1.0	—	100	0.24	0.44	—	—

*Tetrapropyl dithiopyrophosphate.

**Topical application, in acetone, measured drop method.

***Application by turntable modification of Peet-Grady Method; as concentration of spray mg malathion etc./cc to give 50% kill in 24 hrs.

†3 days old laboratory reared adults average wgt. ♂ 6.89 mg, ♀ 7.35 mg.

††LD₅₀ estimated from dose-mortality curve.

(4) Toxicity of malathion and other compounds vs. Protoparce sexta (larva) by topical and oral exposure; S = small larvae (2nd, 3rd instar) wgt. 0.9(0.6-1.1)g, M = medium larvae (3rd, 4th instar) wgt. 2.5(1.2-4.0)g, L = large larvae (5th instar) wgt. 5.4(4.1-7.5)g: 1306

Insecticide	LD₅₀ topical (μg/larva)			LD₉₀ topical (μg/larva)			LD₅₀ oral (μg/larva)	LD₉₀ oral (μg/larva)
	L	M	S	L	M	S	L	L
Malathion	481	61	23.6	1276	553	92	365	1,621
Parathion	52	9.9	2.8	183	64	12.3	15.7	54
Endrin	42	2.9	0.51	219	6.3	6.3	9.9	49
Isodrin	87	7.6	3.0	490	29	56	15.3	138
Lindane	206	—	—	1235	—	—	209.0	398
Dieldrin	482	—	—	2559	—	—	—	—
Aldrin	487	—	—	1359	—	—	—	—
Heptachlor	1058	—	—	4005	—	—	—	—
Toxaphene®	1363	32	30	5778	138	112	143	6,025
DDD	2622	376	37	9813	2620	367	878	3,192
DDT	≫4000	2334	366		9887	1342	4416	28,040

(5) Toxicity of malathion and others vs. mosquitoes:

(a) Vs. DDT-R Aëdes nigromaculis and Culex tarsalis (larvae, 4th instar). 1193

Insecticide	LD₅₀ 24 Hrs. (ppm) Aëdes	Culex
Malathion	0.025	0.0185
EPN®	0.000862	0.000649
Tetra-n-propyl dithionopyrophosphate	0.0625	0.0178
DDT	0.0588	0.111

(b) Vs. Anopheles quadrimaculatus (larva, 4th instar); laboratory tests using acetone-water suspensions: 1766

Insecticide	% Mortality In 48 Hrs. At							
	0.1 ppm	.05 ppm	.025 ppm	.01 ppm	.005 ppm	.0025 ppm	.001 ppm	.0005 ppm
Malathion	100	100	96	80	80	60	40	24
Sulfotepp	100	100	100	100	100	100	74	34
Parathion	100	100	100	100	100	96	56	34
EPN®	100	100	100	100	100	96	32	—
Methyl parathion	100	100	100	100	100	67	—	—
O,O-dimethyl O-(2-chloro-4-nitrophenyl) thiophosphate	100	100	100	96	86	62	62	44
Ethyl o-nitrophenyl thiobenzene phosphonate	100	100	100	100	70	80	4	—
Diazinon	100	100	100	100	36	20	—	—
Para-oxon	100	100	100	82	50	—	—	—
Dipterex®	100	100	100	64	46	24	—	—
Chlorthion®	100	100	88	76	44	—	—	—
Potasan®	100	98	56	30	5	—	—	—
O,O-diethyl O-piperonyl thiophosphate	100	94	58	26	—	—	—	—
NPD	94	—	62	30	—	—	—	—
DDT	—	—	—	100	94	49	24	—

(c) Vs. Anopheles quadrimaculatus (adult, 4 days old) by topical application; insecticides in ethanol solution: 2051

Insecticide	LD_{50} (μg/insect)		LD_{90} (μg/insect)		Relative Effectiveness (DDT = 1.0) At			
					LD_{50}		LD_{90}	
	♂	♀	♂	♀	♂	♀	♂	♀
Malathion	.0087	.0095	.019	.022	2.3	7.0	2.4	5.9
p,p'-DDT	.02	.066	.045	.13	1.0	1.0	1.0	1.0
p,p'-DDD	.041	.1	.098	.22	.49	.66	.46	.59
Methoxychlor (tech.)	.035	.1	.078	.22	.57	.66	.58	.59
Chlordane	.105	.24	.19	.46	.19	.28	.24	.28
Dieldrin	.009	.023	.022	.048	2.2	2.9	2.0	2.7
Lindane	.0085	.011	.032	.042	2.4	6.0	1.4	3.1
Toxaphene®	.15	.29	.29	.5	.13	.23	.16	.26
Allethrin	.0029	.008	.013	.041	6.9	8.3	3.5	3.2

(6) Malathion and other compounds in baits (sugar and molasses solutions) for control of Musca domestica: 1915

Insecticide	Laboratory Tests % Down or Dead In			Field Evaluation (Control After 24 Hrs.)
	30 Min.	1 Hr.	24 Hrs.	
Malathion 1%	43	56	93	Excellent Control
Aldrin 1%	20	76	100	—
BHC 1%	43	76	100	—
Dipterex® 0.1%	54.5	56.5	100	Excellent Control
Chlordane 1%	10	20	100	—
Chlorobenzilate 1%	0	0	60	—
DDT 1%	30	44	98	Unsatisfactory control
CS-708 1%	13	20	80	Fair control
Diazinon 1%	23	36	96	Excellent control
Dieldrin 1%	20	66	100	Unsatisfactory control
Heptachlor 1%	6	48	100	" "
Lindane 1%	3	6	100	" "
Lethane® 384 1%	0	0	0	—
Metacide 1%	23	23	100	—
Methoxychlor 2%	23	20	93	Unsatisfactory control
NPD 1%	36	40	90	—
Parathion 1%	13	13	90	—
Strobane® 1%	10	36	96	—
TEPP .5%	53	56	100	—
Toxaphene® 1%	40	56	100	Unsatisfactory control
Borax (saturated)	0	0	33	—
Boric acid 0.63%	3	3	50	—
$CnSO_4$ 2%	0	0	36	—
Formalin 2%	16	16	30	—
Cryolite 1%	0	0	0	—
NaF 2.5%	0	0	66	—
Rotenone 1.3%	0	0	50	—

**For other data on fly control by Malathion, see Diazinon.

(7) Malathion and other compounds vs. ectoparasites of livestock and poultry:

(a) As a spot treatment vs. Haematopinus eurysternus on cattle (used variously as emulsifiable concentrate and wettable powder formulations); as dips for Bovicola caprae and Bovicola limbatus on goats; on chickens as dusts (in kaolin) vs. Eumenacanthus stramineus: 2862

Insecticide	Vs. Haematopinus			Vs. Bovicola		
	Conc. (%)	% Kill 24, 48 Hrs.	Wks. Effective	Conc. (%)	% Kill 24, 48 Hrs.	Infestation After 4 Wks.
Malathion	.5	100	2	.25	100	0
"	.05	100	1	.1	100	0
"	—	—	—	.05	100	0
"	—	—	—	.025	100	0
DDT	.5	100	4	0.25	100	0
"	.25	100	3	—	—	—
Toxaphene®	.5	100	4	—	—	—
Strobane®	.5	100	4	.2	100	0
"	—	—	—	.1	100	0
Parathion	.05	100	3	—	—	—
"	.01	100	3	—	—	—
"	.005	25	0	—	—	—
Chlorthion	.25	100	1	.002	100	0
Dipterex®	.25	100	1	.1	100	light
"	.1	100	0	.05	100	"
"	—	—	—	.025	100	"
"	—	—	—	.01	100	"
"	—	—	—	.002	100	"
Bayer 21/199	.25	100	2	.002	100	0
"	.2	100	2	—	—	—
"	.1	100	1	—	—	—
"	.05	100	1	—	—	—
Diazinon	.25	100	2	.05	100	0
"	.1	100	2	.025	100	0
"	.05	100	1	.01	100	0
"	.01	95	1	.005	100	light
"	.005	25	1	—	—	—
"	.002	5	1	—	—	—
Pyrazinon	.25	100	3	—	—	—
EPN®	.05	100	1	.002	100	0
"	.01	100	1	—	—	—
"	.005	100	1	—	—	—
"	.002	25	0	—	—	—
Tetrapropyl dithiopyrophosphate	.05	100	1	—	—	—
Endrin	—	—	—	0.05	100	0
Isodrin	—	—	—	0.05	100	0
Bayer 21/200	—	—	—	0.002	25	light

Malathion, lindane and diazinon at 1%, DDT, toxaphene, Strobane®, chlordane, methoxychlor and DDD controlled completely original infestations of Eumenacanthus on chickens, used as dusts; all were effective for 4 wks. save methoxychlor, lindane, malathion, diazinon, in the case of which light reinfestations were noted in 2 to 4 wks.

(b) As a 4% dust, malathion controlled the northern fowl mite, Bdellonyssus sylviarum, when used on the bodies of fowl by individual dusting, or in the litter of nests: 1390

(c) Malathion, at 0.5 and 1.0% sprayed on swine at 1 quart per pig vs. Sarcoptes scabiei suis (sarcoptic mange of swine) yielded complete recovery from mange by the 19th day after treatment without toxicity for swine. 2582

(d) Malathion controlled chicken red mites and northern fowl mites, when applied as 4% dusts at 1 lb/20 ft^2 to floor litter, roosts, droppings, nests. Avoid food and water contamination. 2802

Malathion and Beneficial Insects:

1) For the honeybee, Apis mellifera, malathion is considered extremely hazardous when applied to plants in bloom which are frequented by bees. See, in this work, the section titled, Bees and Insecticides.

2) Vs. Collops vittatus, Hippodamia convergens and Coleomegilla maculata (adults) placed on plants previously treated by the vacuum dusting method: 1404

Insecticide and Concentrations	% Mortality In 24 Hrs. Of		
	Collops	Hippodamia	Coleomegilla
Malathion 5%	47	90	100
Chlorthion® 5%	64	82	100
Diazinon 4%	37	66	100

Insecticide and Concentrations	% Mortality In 24 Hrs. Of Collops	 Hippodamia	 Coleomegilla
Parathion 2%	65	78	98
DDT 5%	38	6	32
Perthane® 5%	23	6	12
Strobane® 5%	10	18	12
Heptachlor 2.5%	41	30	38
Toxaphene® 10%	32	12	36
Endrin 1%	27	10	18
Dieldrin 2%	36	4	24
Control	11	4	0
Lowest Sig. Diff. 5% level	20	24	26

For Comparative data concerning the effectiveness of malathion and other acaricides see the tabulations in the section of this work titled, Miticides or Acaricides.

3) Pharmacological, pharmacodynamic, physiological, etc.; insects:

a) Mode of action: (Also see recent data under Addenda).

(1) Malathion in vitro and malathion and/or its metabolites in vivo inhibits the activity of choline esterase(s) active in the hydrolysis of acetylcholine which is all important in nerve transmission of higher animals. 2231 713

(2) Acetylcholine and acetylcholine esterase(s) occur in insect nervous systems. The role of acetylcholine in neural transmission is less well-defined than it is in mammals and other vertebrates, but its presence in abundance in brain and nerve cord presupposes a role of importance in insect nerve physiology. 2231

(3) While evidence does not seem to support acetylcholine in the role of neural synaptic mediator in insects, it has been proposed that non-choline ester(s) may be, in insects, the synaptic mediator(s) and that these are decomposed by an enzyme(s) capable also of hydrolyzing acetycholine and being inhibited by substances which inhibit acteylcholine esterase(s). 2231

(4) In the inhibition of choline esterase, malathion is less active in vivo than many other organic phosphates and (both in insects and in vertebrates) a metabolite is considered to be the truly potent toxicant in this respect.

b) Metabolism of malathion in insects: (See the data on the metabolism of malathion in higher animals in this section). 2092 2231

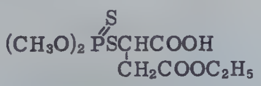
(1) The schema of possible metabolism proposed for higher animals is believed applicable to Periplaneta americana.

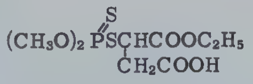
(2) It is suggested that the metabolic inactivation and/or elimination of malathion is less extensive, complex, and effective in insects thus accounting for the discrepancy in toxicity shown for insects and that for higher forms. For example, hens given malathion intraperitoneally show the definite initial symptoms of intoxication, but even 200 mg/k do not prostrate or kill. This is taken to indicate a high elimination and inactivation activity (and possibly poor absorption at the ultimate action site).

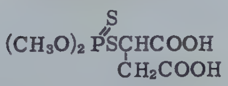
c) Toxicity and anti-choline esterase activity of malathion and some putative metabolites for insects: 2092

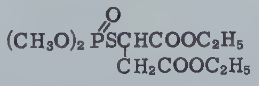
Compound	LC_{50} (%, w/v) For Citrus Red Mite	 Thrips	 Mosquito Larvae	LD_{50} Topical For Musca (μg/fly)	ID_{50} Musca Head Choline Esterase
I Malathion	0.0042	0.00016	<0.00001	0.6	7×10^{-5}M
II or III (half ester)	>1.0	>1.0	.00035	>10	3×10^{-5}M
IV (Di acid)	>1.0	>1.0	$>.01$	>10	$>1 \times 10^{-4}$M
V (Thiolphosphate)*	0.0032	0.000018	–	ca. 0.6	1×10^{-7}M

*putative active metabolite (toxic action)

II =

$(CH_3O)_2\overset{S}{\overset{/\!/}{P}}S\underset{CH_2COOC_2H_5}{\underset{|}{C}}HCOOH$

III =

$(CH_3O)_2\overset{S}{\overset{/\!/}{P}}S\underset{CH_2COOH}{\underset{|}{C}}HCOOC_2H_5$

IV =

$(CH_3O)_2\overset{S}{\overset{/\!/}{P}}S\underset{CH_2COOH}{\underset{|}{C}}HCOOH$

V =

$(CH_3O)_2\overset{O}{\overset{/\!/}{P}}S\underset{CH_2COOC_2H_5}{\underset{|}{C}}HCOOC_2H_5$

d) Action on cytochrome oxidase:

(1) Organic phosphates, notably TEPP, stimulate cytochrome oxidase of Periplaneta americana coxal muscle in in vitro systems, as measured by O_2 uptake in the Warburg apparatus, at molar concentrations of 10^{-3}, 10^{-5}.

(2) Malathion and parathion, however, completely inhibit cytochrome oxidase in the system noted above at 10^{-3}M.

e) Effects of temperature and the pyrethrin synergist, piperonyl butoxide (PBO), on the action of malathion vs. DDT-R ("Campus" biotype) and DDT- non R ("KUN" biotype) Musca domestica (4 day old adult ♂ insects). Treatment by topical application in acetone solution; PBO to malathion ratio = 10:1; mortality determined at 24 hrs. after treatment; LD_{50} values are for malathion. 2575

Temperature (°F)	"Campus" (DDT-R)						"KUN" (DDT-non R)					
	Malathion			Malathion + PBO			Malathion			Malathion + PBO		
	LD_{50} μg/g	Fiducial Limits 95%	Slope	LD_{50} μg/g	Fiducial Limits 95%	Slope	LD_{50}μg/g	FL 95%	Slope	LD_{50}μg/g	FL 95%	Slope
63	30.12	26.85-33.65	6.23	50.79	38.02-62.81	3.25	18.80	18.39-20.53	9.22	34.66	30.89-45.58	6.04
70	26.44	22.34-27.33	7.24	38.56	34.44-43.55	5.74	17.57	13.81-17.62	15.87	24.54	23.52-28.11	8.49
78	20.75	19.41-21.63	12.41	30.71	27.38-34.28	5.85	12.87	11.93-13.43	10.92	18.83	16.7 -26.66	3.15
82	19.56	17.86-23.88	4.48	34.66	31.99-37.76	7.97	13.39	12.63-14.79	8.26	19.43	17.32-21.38	7.62

(1) Temperature and toxicity of malathion vs. both DDT-R and DDT-non R Musca are indicated as directly related.

(2) An antagonism is indicated between piperonyl butoxide and malathion topically applied both in case of DDT-R and in case of DDT-non R Musca.

f) Effect of piperonyl butoxide on malathion action: 2576

(1) PBO diminished (antagonized) the toxic action of malathion on both DDT-R and DDT-non R biotypes of Musca domestica, topically treated.

(2) In vitro malathion inhibition of choline esterase systems (DDT-R and DDT-non R Musca ChE and bovine erythrocyte ChE) was sharply decreased wherever PBO was used with malathion, the effect being more pronounced for true ChE (acetocholine esterase) from bovine erythrocytes than for Musca ChE.

(3) In vivo PBO, applied topically before malathion topical treatment, yielded protective effect for Musca domestica; topical PBO applied 6 hrs. after topical malathion yielded protection of ChE from malathion, although no protective effect followed if a 16 hr. interval between PBO and malathion applications was allowed.

(4) By contrast PBO synergized Diazinon and Dipterex® (Bayer L 13/59), markedly enhancing their lethal effect on Musca. PBO exerted no effect on the in vitro anti-ChE activities of Diazinon or Dipterex®.

Miscellaneous Remarks:

1) Tested vs. Sitophilus granarius, S. oryzae, Rhizopertha dominica, as dusts or sprays applied to whole kernel wheat of 10% moisture contact, high mortality was recorded at dosages as low as 2 ppm after 3 months storage. Dusts were particularly effective; 6-7 mos. after application at 8-16 ppm malathion treatment was still effective. No evidence of breeding was noted 4 mos. after treatment at dosages yielding 100% kills of adults. Rhizopertha proved most resistant, S. oryzae most susceptible to malathion. 2004

2) Vs. Aonidiella aurantii: Effective (California) for light-moderate infestation, provided dosages exceed 2 lbs (25% wettable powder)/100 gallons applied during the immediate post-blooming period. May be used with parathion and petroleum oil. Does not bring about increase in infestations of insects or acarines for which it is ineffective. 473

3) 2.5, 5.0% emulsions + 12% sugar, as residual deposits, yielded good fly control lasting from 1-3 wks. 2.5% 1794
suspensions yielded good control for 1 week vs. DDT-R Musca domestica in dairy trials. 1092

4) The manufacturer provides spray and other treatment schedules and data on economic insects for which malathion is effective.

Addenda; recently published data on malathion:

1) Toxicity of malathion for chickens, turkeys, and their ectoparasites: 1088
   a) 9 month old chickens, 12-15 week old turkeys, survived dipping in 1% malathion preparations; chickens may show symptoms.
   b) 2% malathion dips killed 25% of tested turkeys (with symptoms in other treated subjects).
   c) 4% malathion dips killed all tested birds including a goose; dead birds showed little overt pathology.
      ① 3% emulsions effectively controlled Menacanthus stramineus when used as roost sprays.
      ② 3% emulsions as sprays were effective vs. Argas persicus only if the tick remained on the treated surface for 9 hours (immediately after treatment) to 34 hrs. (2-4 weeks after application).
      ③ 3% emulsion sprays eradicated Dermanyssus gallinae.

2) Malathion as a litter treatment and nest treatment to control Menacanthus stramineus (body louse of chickens): 1391
   a) Litter treatments with 4% malathion dusts at 0.5, 0.25, 0.2 and 0.1 lb/20 ft^2 yielded excellent initial control; using 0.5 and 0.25 lb. dosages control could be extended for 5 weeks at least.
      (1) No effects observed on the hatching qualities of eggs nor were malathion residues to be found in egg whites or yolks of eggs laid in treated nests, or directly smeared with the insecticidal preparations tested.

3) Malathion vs. Dermanyssus gallinae, Menopon gallinae, Goniocotes gallinae, Eumenacanthus (= Menacanthus) stramineus in field tests: 2581
   a) Sprays containing malathion at 1% applied to walls, ceilings, roosts, nests of chicken houses at 1 gallon/1000 ft^2, and 4% malathion dusts applied to litter at 1 lb/20 ft^2 both yielded complete control, save in one house from which the chickens were excluded during spraying.

4) Malathion as an insecticide in "bait stations" for the control of Musca domestica in dairy barns, poultry houses, hog pens, field lots and farms (Florida, Kansas, Nebraska tests): 1764

a) 2% malathion (and 2% Dipterex® [Bayer L13/59] baits yielded excellent control in situations where a sufficient number of stations was established and sanitation maintained to a "fair degree," at least. The effectiveness of the baits endured for from 28 to 98 days.

b) Chlorthion® and American Cyanamid Experimental 4124 at 2% yielded good control in limited tests.

5) Malathion and its isomer; inhibition of choline esterase and succinic oxidase by: 2391

a) Effect of malathion in vivo by injection in Periplaneta americana.

(1) LD_{50} malathion = 8.4 μg/g; LD_{50} of iso-malathion (prepared by 3 hr. heating at 150°C of malathion in a sealed vial, the product being taken up in chloroform) = 60 μg/g.

(2) Isomalathion (prepared as above) at 50 mg/k, intravenous, in mice yielded no toxic symptoms.

b) Malathion poisoning in Periplaneta americana: Hyperexcitability followed by complete ataxia with marked tremor initially of the whole body, later of the limbs only; onset of ataxia in 0.5 to 1 hr. after treatment but extraordinarily prolonged in duration (at 10 μg/g doses some insects persisted in a moribund state for 5 days following injection and remained capable, on stimulus, of intermittent tremors; a similar condition endured for 4 days after 100 μg/g doses with no recoveries however in either instance). By contrast, it may be noted that in TEPP poisoning death ensues within 5 to 10 minutes of injection, following a hyperexcitable phase of great violence.

c) Respiration of Periplaneta following injected malathion: At doses of 17 to 96 μg/g O_2 uptake was not markedly increased, although initially during the first 6 hrs. (ca.) marked peaks and troughs in the graph of O_2 uptake were noted.

d) Choline esterase levels in nerve cords of malathion poisoned Periplaneta:

①

Dose (μg/g)	Condition, 5 Days After Injection	μl CO_2/Nerve Cord In 30 Min Of ChE Assay	% Inhibition Of ChE
0	alive	27	0
4.3	alive	21	22
8.5	alive	20	26
43	alive	15	44
43	alive	14	48
85	alive	17	37
85	alive	25	7

②

Compound	Dose (μg/g)	μl CO_2/Nerve Cord In 30 Min. Of ChE Assay	% Inhibition Of ChE 5 Hrs. After Injection
Control	0	36	—
TEPP	10	1.9	96
TEPP	1	2.9	20
Malathion	85	5.9	84
Malathion	9	15	58

③ Choline esterase inhibition in Periplaneta nerve cords following injected malathion at 50 μg/g:

Time After Injection (hrs.)	μl CO_2/Nerve Cord In 30 Min. Assay	% Choline esterase Inhibition
2	14	61
24	28	22
48	29	19
72	29	19
96	28	22
Control	36	—

e) Interpretation and summary:

(1) Malathion in insects yields signs of neurotoxic action.

(2) Patterns of activity (respiration, ChE levels) following poisoning with typical anti-ChE agents differ from those yielded by malathion namely: Long pre-lethal period, no stimulation of respiration, only temporary inhibition of nerve cord ChE with first death only at the level of 57% ChE inhibition.

(3) Heat isomerization of malathion to S-methyl thiolphosphate yields iso-malathion.

(4) Symptoms of malathion poisoning in Periplaneta americana are atypical of usual organic phosphate poisoning, viz., choline esterase (nerve cord) shows sharp preliminary decrease followed by a gradual increase until death.

(5) Succinic oxidase is but slightly inhibited by malathion (it must be kept in mind that levels of this enzyme decline if insects (post-mortem) are held at room temperature) although the ChE level remains constant.

(6) Iso-malathion in vitro reveals itself a more potent ChE inhibitor than malathion in the cases of human serum and human erythrocyte ChE, fly ChE, mouse liver succinic oxidase and fly succinic oxidase.

(7) In vitro evidence yielded by malathion supports lethal action by anti-ChE activity but in vivo results present anomalies. However, in Periplaneta succinic oxidase inhibition is probably not the death mechanism in malathion poisoning.

6) Malathion and others, comparative toxicity for Heliothis zea and Heliothis virescens 6th instar larva at 240-450 mg weight. Toxicants as topical applications in methyl ethyl ketone solution applied to the abdominal dorsum: 1124

Toxicant	LD$_{50}$ (μg/g) For	
	Heliothis zea	Heliothis virescens
Malathion	130	160
Toxaphene®	2000	18,000
DDD	3000	17,000
DDT	3000	6,500
Endrin	17	180
Dipterex®	30	60
Bayer 17147	40	54
Shell OS-2046	4.8	4.8

7) Malathion vs. Argas persica (Fowl Tick); Rodriguez Jr., J. L., and Riehl, L. A., The Journal of Economic Entomology 50(1): 41, 1957:
   a) As an aqueous spray (prepared from 57% emulsifiable liquid formulation) containing 1.0% actual malathion, applied under high pressure to the inside and outside of poultry houses, and to floor litter, with particular attention to areas behind wall boards, timbers, under joists and studs and roofing material, in cracks of the structure, yielded complete control of Argas persica by the 49th day after application following a progressive decline in tick numbers to the period of complete suppression of infestation.

8) Malathion dust by self-treatment in control of Menacanthus stramineus of chickens, Rodriguez Jr., J. L., and Riehl, L. A., The Journal of Economic Entomology 50(1): 64, 1957.
   a) Malathion dusts at 1, 2, 4, 10% active malathion applied by hand to whole surface of floor litter of poultry pens or to "wallows" or dust-bath boxes so that distribution to the birds was by self-administration in the course of normal activity (chiefly by dust-bathing) yielded the following results:
      (1) No lice found after dust applications in concentrations as low as 2% malathion within 70 days when dosage was at 1 lb/20 ft^2 entire floor litter surface.
      (2) No lice found within more than 44 days after application of dust at 10 lbs/pen applied to dust "wallows" only (4 lbs/100 fowl).
      (3) Control of lice for more than 35 days obtained with malathion concentrations in dusts as low as 4% applied at 2-3 lbs. dust/pen in dust-bath boxes (1 lb/100 fowl).

9) Malathion and Isomalathion; effects on carbohydrate metabolism in mouse, Periplaneta americana, and Musca domestica; O'Brien, R. D., The Journal of Economic Entomology 50(1): 79, 1957:
   a) In mouse brain homogenates (system of Le Page, G. A., Journal of Biological Chemistry 176: 1008, 1948) malathion and isomalathion (O,S-dimethyl S-(1,2-dicarboethoxyethyl) phosphorodithiolate) effectively inhibited pyruvate oxidation by a possible interference with the citrate oxidation system.
   b) With exception of the above inhibition, the glycolytic and tricarboxylic acid cycle mechanisms in mouse, Periplaneta, Musca were not, in vitro, materially inhibited by malathion, isomalathion.
      (1) Inhibition of insect enzymes generally less than inhibition of mouse enzymes.
      (2) Malathion being far more toxic for insects than for mammals, it was considered unlikely that the interferences with carbohydrate metabolism observed in vitro played any role in the insecticidal action of the toxicant in vivo.

118

MERCUROUS CHLORIDE (Calomel; Mercury mono-, proto-, or sub-Chloride; Mild Mercury Chloride; Precipité Blanc.)

$HgCl$ Molecular weight 236.07

GENERAL [Refs.: 2231,2120,1196,1195,484,1544,128,470,880]

A substance long known for insecticidal properties, particularly useful in control of Anthomyids (root maggots) of cabbage, cauliflower, other crucifers, onions etc. Applied either to the soil, or used as a prophylactic seed dressing. Not more effective than mercuric chloride (corrosive sublimate), but less hazardous because of a very low solubility which permits the use of rather heavy suspensions in water. Possesses fungicidal properties useful in protection of turf, and in control of cabbage (and other crucifer) club roots. The toxicity and hazard for mammals and other higher animals are considerably less than those of mercuric chloride. Has also been tested, with some promise, as an ovicide for *Lucilia sericata*, the sheep blowfly.

PHYSICAL, CHEMICAL

A white powder without odor or taste; sublimes without melting at 400°-500°C (732°-932°F); b.p. 383°C; specific gravity 7.15; virtually insoluble in water, alcohol, ether; in water dissolves to the extent of 0.002 g/l at 18°C; slowly decomposed by light to metallic mercury and mercuric chloride, the latter vastly increasing the toxic hazard of the exposed salt; alkalis and alkaline earth chlorides increase the solubility while enhancing the decomposition; incompatible with many substances, including bromides, iodides, sulfates, sulfites, copper and lead salts, soaps and sulfides.

- a) Formulations: As dusts (4%) in such inert carriers as gypsum and slaked lime; as aqueous suspensions applied to the soil.

TOXICOLOGICAL

1) Toxicity for higher animals:
   - a) Not readily absorbed by the body because of its insolubility, and consequently less toxic than mercuric chloride. 851 289
     - (1) Ease of oxidation by exposure to light or bacterial action, with the production of mercuric chloride, makes it a source of intensely toxic mercuric ion, Hg^{++} (ca. 1 g of $HgCl_2$ is considered a lethal dose for man).
     - (2) Metallic mercury and Hg^{++} are concentrated in the kidney and deposited to a lesser extent in other tissues.
   - b) Mercurous chloride, *per se*, is harmless, but the bivalent mercury ions which may be present or arise account for its toxicity. Administration may lead to systemic mercury poisoning. 404
     - (1) Toxicity is not related to the amount ingested but to length of time in which the substance is retained in the intestine. The failure of ingested calomel to bring about catharsis is a danger sign of potential poisoning.
     - (2) The average dose of calomel (used therapeutically) is 0.1 g for human beings, and is almost invariably given with a saline cathartic.
   - c) Excretion of mercury from the body is fairly rapid. 851
   - d) Mechanism of action: 851
     - (1) The mercuric ion interacts rapidly with protein, producing denaturation.
     - (2) Inhibition of cellular enzymatic activity; SH enzymes are particularly sensitive.
     - (3) Mercuric (Hg^{++}) intoxication may produce deep shock and death from circulatory collapse. The heart is directly affected, with arrhythmias and ventricular fibrillation being present.
     - (4) Stomatitis, gum discoloration, and soreness may be noted.
     - (5) Renal damage is the usual cause of delayed death from mercury poisoning.

2) Phytotoxicity:
   - a) Strongly phytotoxic; use limited to soil and seed application.

3) Toxicity for insects:
   - a) Vs. *Hylemyia antiqua*, *H. brassicae*, *H. floralis* by treatment of seeds or seedlings effective control may be obtained. 470 880
   - b) Useful in the control of fungus gnats.
   - c) Sheep, treated with calomel (dusts, dips), have a fleece toxic to eggs of *Lucilia sericata*. 1544
     - (1) The active principal in this effect is reported as volatile, and apparently is mercury vapor.
     - (2) Calomel is activated by wool, and its accompanying substances and components.
     - (3) The ovicidal effect does not require contact with the eggs; the effect is that of a toxic gas. First instar larvae of *Lucilia sericata* are not killed by the putative toxic vapors.
     - (4) Pastes of calomel and water are ineffective; the activating effect of wool is necessary and the effect is greater at 37°C than at 23°C.

119

METHANESULFONYL FLUORIDE (M.S.F.; Fumette.)

H_3CSO_2F

GENERAL [Refs.: 2128,283,976,717]

A fumigant highly effective for greenhouse use, but with an exceedingly high toxic hazard for man. In spite of the toxicity it has been recommended as a fumigant for ectoparasites of domestic animals.

PHYSICAL, CHEMICAL

A colorless liquid of rather pleasant odor; not flammable; b.p. 121°-123°C; slightly soluble in water (5% at 22°C). 2120
Produced by the reaction of methane sulfonyl chloride and potassium fluoride. 717,2774

a) Formulation: As an ingredient of smoke-producing, insecticidal pyrotechnic mixtures.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) A powerful toxicant, but less toxic by inhalation than by subcutaneous or parenteral injection. Dogs survive 1 minute exposures to 23 g/m^3; rabbits survive 1 minute exposures to 3 to 6 g/m^3. 2120 283,976

Mouse	sc	LD	3.5 mg/k
Rat	sc	LD	3.5 mg/k
Rabbit	sc	LD	3.5 mg/k
Dog	sc	LD	3.5 mg/k

2) Phytotoxicity:
   a) No phytotoxic hazard at insecticidal concentrations. 2120

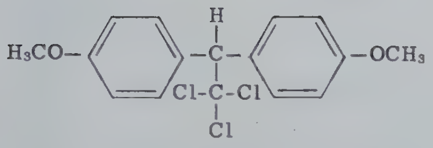
3) Toxicity for insects:
   a) No quantitative data available to this compilation at time of preparation.

4) Related compound: Trichloromethane sulfonyl chloride vs. Tribolium confusum. 2626
   a) The saturation concentration at 25°C = 8.3 mg/l.
   b) Concentration for 50% kill, 5 hrs. exposure, 25°C = 5.7 mg/l.
      Concentration for 90% kill, 5 hrs. exposure, 25°C = 8.3 mg/l.
      1 to 2.5 hrs. exposures at 8.3 mg/l yielded 24.3% kills at the end of 20 days.

120

METHOXYCHLOR

(2, 2-bis-(p-Methoxyphenyl)-1, 1, 1-trichloroethane; 1, 1, 1-Trichloro-2, 2-bis-(p-methoxyphenyl) ethane; 2, 2-Dianisyl -1, 1, 1-trichloroethane; 2, 2-Di-p-anisyl-1, 1, 1-trichloroethane; DMDT; Methoxy-DDT; Marlate®2-MR [formulation containing 24% tech. methoxychlor]; Marlate® 50 [wettable powder formulation containing 50% tech. methoxychlor].)



Molecular weight 345.65

GENERAL [Refs.: 353,2231,1801,2120,129,2815,757,1059,3199,1933,818,1880,1881,3156,3161,408,1863,235, 3085,546,946,3277,407,1966,1948,3151,3074,875,664,3255,2571,2545,2543,2833,767]

An important insecticidal analogue of DDT in which the p,p' chlorines of DDT are replaced by methoxy-groups. Methoxychlor retains to a great extent the toxicity for insects which characterizes DDT, all in having specific excellences of its own, while being from $\frac{1}{25}$th to $\frac{1}{50}$th as toxic for mammals as is DDT. Methoxychlor does not accumulate in the fat of animals, nor is it excreted in milk, to the extent characteristic of DDT. Methoxychlor finds especial value for use on livestock, domestic animals, and animal forage crops. It retains to a high extent the residual toxicity for insects of DDT with a low residue hazard to man and higher forms. Methoxychlor may be applied to crops up to 7 days before harvest. Effective against a wide range of insects damaging to fruits, vegetables, ornamentals, forage crops, livestock, domestic animals and human beings. For Epilachna varivestis and Conotrachelus nenuphar methoxychlor is more effective than DDT; vs. the European corn-borer and the cotton bollworm it is less effective than DDT. Toxicity for aphids, and acarines, is (on the whole) of a low order. One of safest of all insecticides.

PHYSICAL, CHEMICAL [Refs.: 2970,2766,353,2231,3199,643,818,3203,2221]

Solid, in colorless dimorphic crystals (pure state); crystals melt at 78°-78.2°C and 86°-88°C depending on crystal type; $d_{4°}^{25°}$ 1.41; the odor is fruit-like; the effective insecticidal agent is the p,p'-isomer (the o,p'-isomer is present in technical methoxychlor to the extent of ca. 12%, the balance being p,p'-isomer; setting point (technical) = 69°C; not flammable at ordinary temperatures; virtually insoluble in water; readily soluble in some organic solvents (particularly aromatics) for example, soluble in trichloroethane at 70 g/100 cc at 20°C, in methylene chloride at 133 g/100 cc at 15°C; moderately soluble in olive oil, alcohol, petroleum oils; stable toward heat; resists oxidation; less susceptible than DDT to alkaline hydrolysis; stable toward ultra-violet light; slowly dehydrochlorinated to 2,2-bis-(p-methoxyphenyl)-1,1-dichloroethylene; heavy metals catalyze the dehydrochlorination of methoxychlor as they do that of DDT; long-lasting residual effectiveness; prepared by the condensation of chloral with anisole in presence of sulfuric acid or aluminum chloride.

a) Formulations: Emulsifiable concentrate (24% tech. methoxychlor) as Marlate® 2 MR for use on certain crops, livestock, grain storage bins, space spray vs. flies; water wettable powder at 50% tech. methoxychlor as Marlate® 50 for use as a spray or dip, direct dust to domestic and farm animals, as a spray for buildings, grain storage bins, fruits, garden crops, field and forage crops. The emulsifiable concentrate is incompatible with spray materials, incompatible with oil and should not be applied within 14 days of sulfur or sulfur-product treatment. The wettable powder is compatible with Fermate, Zerlate, Parzate, dithiocarbamate fungicides, copper-A Compound, wettable and dusting sulfurs and EPN-300 insecticide.

TOXICOLOGICAL [Refs.: 3203,2890,3277,407,3359,1966,1948,1449,3151,3074,875,1551,664,3255,2573,1322, 1880,408,1863,2571,2025,235,1552,3085,546,946]

1) General: Orally (Rabbits, Rats) ca. $\frac{1}{4}$th as toxic as DDT; cutaneously ca. $\frac{1}{8}$th as toxic as DDT. When inhaled: 1322
Less toxic than DDT. Acute oral toxicity $\frac{1}{24}$th that of DDT, chronic oral $\frac{1}{6}$th and multiple dermal toxicity $\frac{1}{4}$th 2345
that of DDT.
   a) Man: Estimated danger level single cutaneous application in solution = 169 g; repeated cutaneous application = 36 g/day; estimated fatal dose = 7.5 g/k. 129

2) Residues:
   a) Residue tolerances in parts per million range from 14 ppm for a wide range of fruits, berries, vegetables (leaf, seeds, root) to 3 ppm in fat of cattle, hogs, sheep for human consumption; 100 ppm residue tolerance for alfalfa, clover, cowpeas, forage grasses, peanut forage. 1863

3) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{20}	800	In oil; death in 7 days.	3203
Mouse	or	LD_{50}	> 900	In oil.	3203
Mouse	or	LD_{50}	1850	Produces DDT-like tremors at this dosage.	818
Rat	or	LD_{50} 72 hr	ca. 5000	Tech. product in corn oil; graphic calculation.	1551
Rat	or	LD_{50}	5800	Recrystallized, in corn oil; 10% dead at 72 hrs, 53% in 5 days.	1551
Rat	or	LD_{50}	7000		2890
Rat	or	LD_{50}	6000		1951
Rabbit	ct	LD	> 6000	Daily applications at this dosage (6000) tolerated.	1952 2231
Calf	or	MTD*	500	*=Minimum Toxic Dose.	2567
Cattle	or	MSSD**	500	**=Maximum Safe Single Dose.	3277
Sheep	or	MSSD**	ca. 2000		3277
Sheep	or	MTD*	> 1000		2567
Calf, Cattle, Sheep, Pig, Horse	Dip; Spray	MTD*	>8% concentration	as a single dipping or spray.	2567
Bass	Medium	LC	0.2 ppm	LC DDT = 0.15 ppm.	1937
Bluegills	Medium	LC	0.2 ppm	LC DDT = 0.05 ppm.	1937
Goldfish	Medium	LC_{50}	0.06 ppm	DDT: p,p' 0.06 ppm, o,p' 1 ppm; DDD 0.9 ppm.	1187
Goldfish	Medium	LC_{100}	0.25 ppm	DDT: p,p' 0.25 ppm, o,p' 4 ppm; DDD 2 ppm.	1187
Alaska Grayling		½ as toxic as DDT			3114
Animals	or	LD_{50}	7000	(Average toxicity for all mammals tested;) DDT = 250.	3114
Animals	ct	Danger Level 2820		" " DDT, DDD = 2820.	3114
Chicken (young)	Dip	MTD*	4% concentration	As single dipping.	2571

a) Deaths following high dosages of methoxychlor (in rats) are delayed: 1551

Dosage (g/k)	No. Rats	% Deaths, Cumulative				
		1 day	2 days	3 days	5 days	LD_{50} 72 Hrs. (graph)
2.87 (tech.)	10	0	0	10	—	
4.62 (")	10	0	0	40	—	5 g/k
5.95 (")	15	0	40	53	—	—
2.98 (purified)	10	0	0	10	20	—
4.07 (")	10	0	0	10	20	5 g/k
5.82 (")	15	0	0	7	53	—

4) Subchronic toxicity; short range experiences, feeding tests:

a) Rats: Weanling, 10♂ 10♀/group at 0.01, 0.1, 3.0% in diet for 45 days: 1551

(1) At 0.01% no growth effect; at 0.1% growth retard, real but not marked; at 1% rats in paired feeding tests showed marked growth reduction attributed to a reduced food intake (10 g/day on the 1% methoxychlor diet vs. 15 g food/day for the average rat); at 3% virtually no growth occurred.

(2) No deaths in 0.01, 0.1% groups; 8 of ten in each of the ♂ and ♀ groups died on the 3% diet; the lethal level for 50% kill in 45 days (LL_{50}) was less than 3% methoxychlor in the diet. ♀♀ rats died within week at 10,000 ppm. 1551, 1322

(3) Haemotology (3% group) essentially normal. 1551

(4) At autopsy: 0.01, 0.1% groups no significant difference in organ weights vis-a-vis controls. 3% groups showed uniformly smaller organ weights than controls; in case of testes, decrease in weight was strikingly great. 1551

(5) Histopathology: Heart, lung, spleen, stomach, intestines, liver, kidney, brain, bone marrow, testes: No evidence of histological change save in testis. 1551

(a) Testis: Apparent suppression of spermatogenesis beyond the spermatogonial phase; spermatogonia and Sertoli cells relatively normal; primary spermatocytes variable in number, usually with evidence of necrosis; more mature germ cells absent.

(6) The change in hepatic cells characteristic of DDT, even at low dietary levels, was not noted in methoxychlor-fed rats in the above experiments. 1551

b) Rabbits: After 15 doses 200 mg/k/day: Diarrhoea, anorexia sometimes, with evidences of fatty degeneration of liver, heart; 200 mg/k/day were tolerated for an average of 8 days (4-15) days. 2901, 353

5) Chronic toxicity; higher animals:

a) Rats: Groups of 25 maintained for 2 yrs. on diets with 0.0025, 0.020, 0.16% methoxychlor: 1552

(1) At 0.0025 and 0.020 no effects on growth.

(2) At 0.16% moderate growth reduction. No decrease in life span in any group.

(3) Urine, haematology, organ weights essentially normal; little tendency of methoxychlor to accumulate in tissues.

(4) No histological changes attributable to methoxychlor.

b) Dogs: Groups of 2, maintained 1 year on doses of 20, 100, 300 mg/k/day methoxychlor: 1552

(1) No fatalities as result of treatment; haematology, organ weight, urine essentially normal; no histopathological changes attributable to treatment.

(2) 10,000 ppm toxic to dogs in course of 6 months. 3199, 1949

c) Cutaneous application:

(1) Rats: Repeated application (2,3 cc 30% in dimethyl phthalate) is toxic; paralysis of hind legs, suddenly developing, noted in some. 3199

(2) Multiple applications at 600 mg/k were tolerated by rats (slight irritation). 1949 2573

(3) Repeated exposures of livestock to 1.5% emulsions were found non-injurious. 2573

d) Miscellaneous:

(1) Sheep tolerated 100 mg/k daily oral doses (a comparable daily level of DDT results in marked neural symptoms). 3277

(2) Steers tolerated without effect a single oral dose of 500 mg/k. 3277

(3) Chronic dosage (average of all animals tested) to produce gross symptoms = 5000 ppm (DDT = 100 ppm; DDD = 2500 ppm). 1949

6) Comparative toxicity methoxychlor and DDT; higher animals; oral administration: 1551

Rat

Compound		Dosage (mg/k)	Effects
Methoxychlor		6000 Single dose.	= MLD; isolated livercell necrosis.
"		7000 Single dose.	7 dead/13 tested; diarrhoea, progressive weakness.
"	(tech.)	5000 Single or double dose.	= LD_{50}
"	(purified)	5800 Single or double dose.	1 dead/15 tested in 72 hrs.
DDT		250 Single dose.	= MLD (various workers).
"		180 Single dose.	= LD_{50}
"		150 Single dose.	= LD_{50}

Rabbit

Methoxychlor	200/day 4-15 doses	Death; no neurotoxic effects or liver necrosis; fatty changes in liver; nephrosis, haemosiderosis.
DDT	50/day 15-25 doses	Death; CNS involvement; liver damage.

Rats at various dietary levels

% in Diet	Effects	
	Methoxychlor	DDT
20	Loss of weight; death.	↓
5	No growth; 60% mortality.	
3	No growth; 80% mortality.	
1	Marked growth reduction; no deaths; effect on testis.	
0.5	Lowest level yielding overt effects.	
0.1	Slight growth retard.	Uniformly fatal in 18-20 days; tremors.

7) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:

a) The relative absence of neurotoxic signs at any but highest dosages is noted above and distinguishes methoxychlor from DDT.

b) Metabolism: Not excreted intact, nor as the acetic acid derivative in the urine; a more extensive metabolism is suggested, with anisole groups yielding hydroxyphenyl derivatives; this is in marked contrast to DDT, DDD. 3203

c) The liver as site of methoxychlor metabolism is suggested by feeding to CCl_4-treated animals in which the liver is damaged; in such cases DDT-like tremors develop and deposition in fat and tissues is enhanced. 1932

d) Such tissue and fat storage of methoxychlor as takes place reaches its maximum in 4 weeks; the stored material is mobilized in 2 to 4 weeks when exposure is ended. Rate and completeness of methoxychlor metabolism may account for low storage and accumulation. 3199 2231

8) Phytotoxicity:

a) The phytotoxic hazard of methoxychlor is of a low order. 2120,129,353

b) Apparently harmless to most plants; least injurious to Cucurbitaceae of the chlorinated hydrocarbons, all of which under moist or humid conditions may damage cucurbits. 660

c) Leaves of squash may acquire a transient roughness when exposed to methoxychlor. 660

d) No injury to crops from soil accumulation recorded from applications to 100 lbs per acre. 129

e) Does not cause fruit "russetting" at levels which control curculio, and other orchard insects for which it is effective. 3082

9) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti (larva)	Medium	LC_{50}	0.07 ppm	p,p' DDT = 0.01 ppm; DDD = 0.01 ppm.	1187
Aëdes aegypti (larva)	Medium	LC_{100}	0.2 ppm	" = 0.05 ppm; " = 0.05 " .	1187
Anopheles quadrimaculatus (larva)	Medium	MLC_{100}	0.1 ppm	At 0.05 ppm gave 45% kill.	2020
Anopheles quadrimaculatus (larva)	Medium	LC_{50}	0.01 ppm		767
Anopheles quadrimaculatus (adult) ♂	Topical	LD_{50}	0.035 μg/insect	In ethanol solution [0.57 as effective as DDT].	2051
Anopheles quadrimaculatus (adult) ♀	Topical	LD_{50}	0.1 μg/insect	" [0.66 as effective as DDT].	2051

9) Toxicity for insects (Continued):

a) Quantitative (Continued):

Insect	Route	Dose	Dosage	Remarks	
A. quadrimaculatus (adult) ♂	Topical	LD_{90}	0.078 μg/insect	In ethanol solution [0.58 as effective as DDT].	2051
A. quadrimaculatus (") ♀	Topical	LD_{90}	0.22 μg/insect	" [0.59 as effective as DDT].	2051
Chrysops discalis (adult)	Topical	LD_{50} (est)	30 μg/fly		2707
Chrysops discalis (")	Topical	LD_{90}	90 μg/fly		2707
Conotrachelus nenuphar (adult)	Topical	LC_{50}	4000 ppm	By dipping in water suspension.	2864
Conotrachelus nenuphar (")	Residue	*ME Deposit	865 mg/100 cm^2	*=Minimum Effective Deposit.	2864
Dacus dorsalis (adult)	Topical	LD_{50}	1.0 μg/fly		2692
Fannia canicularis (adult) ♀	Topical	LD_{50} 24 hr.	0.14 μg/fly	In acetone sol.; by measured drop.	1981
Fannia canicularis (") ♂	Topical	LD_{50} 24 hr.	0.12 μg/fly	" ; " .	1981
Musca domestica (adult) ♀	Topical	LD_{50} 24 hr.	0.068 μg/fly	" " .	1981,2692
Musca domestica (")	Topical	LD_{50}	0.07 μg/fly	Laboratory strain; DDT 0.02.	2098
Musca domestica (")	Topical	LD_{50} 24 hr.	0.088 μg/fly	Laboratory strain; at 60°F.	371
Musca domestica (")	Topical	LD_{50} 24 hr.	0.99 μg/fly	" ; at 80°F.	371
Musca domestica (")	Topical	LD_{50} 24 hr.	>100 μg/fly	80°F; 12 generations exposure to methoxychlor.	371
Musca domestica (")	Topical	LD_{50} 24 hr.	1.4 μg/fly	60°F; Pollard (DDT-R) strain.	371
Musca domestica (")	Topical	LD_{50} 24 hr.	0.96 μg/fly	60°F; Bellflower (DDT-R) strain.	371
Musca domestica (")	Topical	LD_{50} 24 hr.	1.0 μg/fly	Bellflower (DDT-R) strain; DDT = 10 μg/fly.	2098,78
Musca domestica (")	Topical	LD_{50} 24 hr.	0.3 μg/fly	Riverside (") " ; DDT = 0.5 μg/fly.	2098,78
Musca domestica (")	Topical	LD_{50} 24 hr.	0.3 μg/fly	Ontario (DDT-R) strain; DDT = 0.5 μg/fly.	2098,78
Musca domestica (")	Topical	LD_{50} 24 hr.	0.3 μg/fly	San José (DDT-R) strain; DDT = 0.7 μg/fly.	2098,78
Musca domestica (")	Topical	LD_{50} 24 hr.	2.3(2.03-2.53) μg/fly	Auburn (DDT-R) strain; 14xs as resistant as Orlando.	2110
Musca domestica (")	Topical	LD_{50} 24 hr.	135.18 μg/g	" ; "	2110
Musca domestica (")	Topical	LD_{50} 24 hr.	1.93(1.33-2.33) μg/fly	Orlando strain (DDT-non R).	2110
Musca domestica (")	Topical	LD_{50} 24 hr.	127.49 μg/g	" " .	2110
Musca domestica (")	Topical	LD_{50} 24 hr.	721.0 μg/g	DDT-I strain, 21 generations selection.	373
Musca domestica (")	Topical	LD_{50} 24 hr.	76.4 μg/g	DDT-W; 3 yrs. exposure (field) to DDT.	373
Musca domestica (")	Topical	LD_{50} 24 hr.	461.2 μg/g	DDT-III; 4 yrs. " " " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	9176.0 μg/g	Methoxy-I; 21 generations selection; methoxychlor exposure.	373
Musca domestica (")	Topical	LD_{50} 24 hr.	14,586.0 μg/g	Multi-I; origin DDT-I; 8 generations selection.	373
Musca domestica (")	Topical	LD_{50} 24 hr.	49.95 μg/g	Laboratory strain I; origin NAIDM; DDT-non R	373
Musca domestica (")	Topical	LD_{50} 24 hr.	50.0 μg/g	" II; origin Univ. of Ind.; DDT-non R.	373
Musca domestica (")	Topical	LD_{50} 24 hr.	1334 μg/g	Multi-III; origin Methoxy-I; 8 generations selection.	373
Musca domestica (")	Topical	LD_{50} 24 hr.	9277.0 μg/g	Multi-IV; " ; 4 " .	373
Musca domestica (")	Topical	LD_{50} 24 hr.	10,444.0 μg/g	Multi-II; " ; 4 " .	373
Musca domestica (larva)	Medium	LC_{25} (ca.)	50 mg/kilo medium	DDT at same dosage gave 100% kill.	1326
Musca domestica (adult)	Topical	LD_{50}	3.4 μg/g	Laboratory strain; DDT-non R.	2094
Cimex lectularius	Contact Spray	LC_{50}	0.55%	In P31 oil, solution sprayed at 0.36 mg/cm^2.	418,419
Pediculus humanus corporis	Contact Spray	LC_{50}	0.9%	" " .	418,419
Heliothrips haemorrhoidalis	Contact Spray	LC_{50}	0.03%		2230
Periplaneta americana (adult) ♂	inj	LD_{50} 96 hr.	7.0 μg/g	In xylene + acetone + deobase + ethanol (10:10:75:5).	558
Periplaneta americana (") ♀	inj	LD_{50} 96 hr.	18.0 μg/g	" " .	558
Rhagoletis cingulata (adult)	Direct Spray Mist	LC_{50} 24 hr.	0.45%	At 75°C; Hoskins-Caldwell Chamber; in water.	1706
Rhagoletis cingulata (")	Direct Spray Mist	LC_{95} 24 hr.	1.27%	" " " .	1706
Rhagoletis cingulata (")	Direct Spray Mist	LC_{50} 24 hr.	0.34%	As above; Parathion + methoxychlor.	1706
Rhagoletis cingulata (")	Direct Spray Mist	LC_{95} 24 hr.	0.96%	" " .	1706
Rhagoletis completa (")	Topical	LC_{50}	0.15 μg/fly		2692

b) Comparative toxicity; methoxychlor and other insecticides:

(1) Methoxychlor and other compounds in bioassay vs. Artemia salina (Brine shrimp), Crustacea; insecticides added to water column in acetone solution; immobilization = sinking to bottom through failure of swimming movements; stages: Adults to nauplii. 2251

Insecticide	Immobilization Time (Min.) At		
	1 ppm	0.1 ppm	0.01 ppm
Methoxychlor	45-60	45-60	45-60
Chlordane	60-120	120-135	120-180
Lindane	45-60	60-120	60-120
Toxaphene	45-60	90-120	18 hrs.
DDT	60	60	60-120
Acetone control (1:100)		24-48 hrs.	
H_2O control		26-50 hrs.	

(2) Toxicity, hydrolysis rate, solubility of methoxychlor and other compounds; test insects = Cimex lectularius, Pediculus humanus corporis: 3288

Insecticide	LC_{50} (Concentration %)		% Hydrolysis After 240 Min.	Solubility (w/v) At 18°C In	
	Pediculus	Cimex		Olive Oil	White Oil
Methoxychlor	0.9	0.55	10	8-10	1-2
p,p'-DDT	0.3	0.53	100	10	2-3
DDD	0.9	1.20	33	10	1-2
Dimethyl-DDT	1.7	3.6	8	18-20	6-8
o,p-DDT (Iso-DDT)	5.5	>20	13	25	10-14
Diphenyl trichloroethane	7.5	>20	10	25-30	10-12
Dichlordiphenylethane	8.5	>20	—	30	25
Dichlordiphenyldichlorethylene	>20	>20	—	14-18	8-10

(3) Methoxychlor and others vs. certain Diptera: Musca domestica (adult ♀), Fannia canicularis (adult ♂,♀), 2707
Chrysops discalis (adult), Anopheles quadrimaculatus (adult (4 day) ♂,♀); Topical application: 2051
1981

Insecticide	**LD_{50} 24 Hrs. (μg/fly)			Chrysops (μg/fly)		Anopheles****			
	Musca ♀	Fannia***				LD_{50} (μg/insect)		LD_{90} (μg/insect)	
		♀	♂	LD_{50}	LD_{90}	♂	♀	♂	♀
Methoxychlor	0.068	0.14	0.12	30	90	0.035	0.1	0.078	0.22
Aldrin	—	—	—	40	170	—	—	—	—
Chlordane	—	—	—	60	650	0.105	0.24	0.19	0.46
DDD	—	—	—	—	—	0.041	0.1	0.098	0.22
DDT	0.033	2.8	1.3	20	250	0.02	0.066	0.045	0.13
Dieldrin	0.031	0.003	0.0026	20	950	0.009	0.023	0.022	0.048
Endrin	—	—	—	9	80	—	—	—	—
Heptachlor	—	—	—	40	200	—	—	—	—
Isodrin	—	—	—	60	170	—	—	—	—
Lindane	0.01	0.76	0.39	4	35	0.0085	0.011	0.032	0.042
Q-137	—	—	—	120	400	—	—	—	—
Toxaphene®	—	—	—	180	480	0.15	0.29	0.29	0.5
Chlorthion®	0.33	0.035	0.022	65	420	—	—	—	—
Diazinon	0.092	0.098	0.054	90	360	—	—	—	—
EPN®	—	—	—	48	120	—	—	—	—
Malathion	0.56	0.1	0.06	130	330	0.0087	0.0095	0.019	0.022
"DCMT"*	—	—	—	90	910	—	—	—	—
Allethrin	—	—	—	—	—	0.0029	0.008	0.013	0.041
Pyrethrins	1.0	0.24	0.44	—	—	—	—	—	—

*O,O-Diethyl (3 chloro-4-methylumbelliferone) thiophosphate.

**By measured drop test; toxicants in acetone solution.

***Average weight (3 day old adults) ♂ 6.89 mg, ♀ 7.35 mg.

****4 day old adults; toxicants in ethanol solution.

(4) Methoxychlor and other compounds: Relative effectiveness compared to DDT (DDT = 1.0) vs. Anopheles quadrimaculatus (4 day old adults) topical application; toxicants in ethanol solution: 2051

Insecticide	Relative Effectiveness (DDT = 1) At			
	LD_{50}		LD_{90}	
	♂	♀	♂	♀
Methoxychlor	0.57	0.66	0.58	0.59
Toxaphene®	0.13	0.23	0.16	0.26
Chlordane	0.19	0.28	0.24	0.28
DDD	0.49	0.66	0.46	0.59
DDT	1.0	1.0	1.0	1.0
Dieldrin	2.2	2.9	2.0	2.7
Lindane	2.4	6.0	1.4	3.1
Allethrin	6.9	8.3	3.5	3.2
Malathion	2.3	7.0	2.4	5.9

(5) Methoxychlor and other compounds vs. 2 strains of Musca domestica (adult); topical application; toxicants in acetone solution; Auburn strain 14 times as resistant to DDT as the Orlando strain (DDT-non R): 2110

Insecticide	Auburn Strain			Orlando Strain		
	LD_{50} (μg/fly)	0.95% Limits	LD_{50} (μg/g)	LD_{50} (μg/fly)	0.95% Limits	LD_{50} (μg/g)
Methoxychlor	2.33	2.03- 2.53	135.18	1.93	1.33- 2.33	127.49
Chlordane	29.0	12.0 -57.0	2791.3	42.0	42.0 -84.0	3586.8
Heptachlor	13.0	11.0 -17.0	855.79	11.0	8.75-15.0	955.68
Chlorthion®	0.14	0.1 - 0.2	10.52	0.21	0.19- 0.25	16.89
Diazinon*	0.06	0.05- 0.07	3.01	0.1	0.09- 0.11	6.15
American Cyanamid 4124	0.03	0.03- 0.03	2.75	0.02	0.02- 0.03	1.73

*In the case of diazinon there was no significant difference in toxicity to the two strains (note overlap of fiducial limits).

(6) Methoxychlor and other insecticides vs. Musca domestica DDT-R and DDT-non R strains; tested by measured drop test; toxicants in acetone solution: 78

Strain	LD_{50} 24 Hrs. (μg/fly)						
	Methoxychlor	DDT	DDD	Toxaphene®	Lindane	Heptachlor	Pyrethrins
Bellflower (DDT-R)	1.0	10.0	20.0	.6	.08	.06	1
San José (")	.3	.7	—	.4	.05	.07	2
Ontario (")	.3	.5	—	.5	.05	.07	2
Riverside (")	.3	.5	—	.5	.06	.07	2
Laboratory (DDT-non R)	.07	.02	.1	.2	.01	.03	1

Insecticide		"Knockdown" Time On Residual Deposits (Minutes) For		
		Bellflower	San José	Laboratory
Methoxychlor 100 mg/ft^2	KD_{50}	255	56	37
"	KD_{100}	360	108	67
DDT 100 mg/ft^2	KD_{50}	720	420	91
"	KD_{100}	2880	1440	152
Lindane 10 mg/ft^2	KD_{50}	11	16	13
"	KD_{100}	15	20	20
Heptachlor 10 mg/ft^2	KD_{50}	40	48	44
"	KD_{100}	52	60	51

(7) Methoxychlor and other compounds vs. Periplaneta americana adult ♂, ♀, by injection (toxicants dissolved in xylene + acetone + deobase + ethanol [10:10:75:5]): 558

Insecticide	LD_{50} 96 Hrs. (μg/g)		LD_{50} ♀ / LD_{50} ♂
	♂	♀	
Methoxychlor	7.0	18.0	2.5
Lindane	0.8	4.4	5.5
Dieldrin	1.0	5.0	5
DDT	4.5	20.0	4.4
Toxaphene®	25.0	80.0	3.2
Chlordane	26.0	52.0	2.0

(8) Methoxychlor and other insecticides vs. Conotrachelus nenuphar (adult); tested by wetting in toxicant + water suspensions: 2864

Insecticide	LC_{50} (ppm)	Ratio To Parathion	Minimum Effective Residue (mg/100 cm^2)	Ratio To Parathion	Field Concentration (ppm)
Methoxychlor	4000	285.7:1	865	25.4:1	1800
Parathion	14	1	34	1	360
EPN®	32	2.3:1	68	2.0:1	390
Dieldrin	104	7.4:1	71	2.1:1	300

(9) Methoxychlor and other insecticides vs. Dacus dorsalis and Rhagoletis completa; topical application to adult insects: 2692

Insecticide	LD_{50} (μg/fly)	
	Rhagoletis	Dacus
Methoxychlor	0.15	1.0
Heptachlor	0.06	.015
Dieldrin	.025	.024
Aldrin	.066	.023
Lindane	.027	.025
Parathion	.011	.012
DDT	.86	.23
DDD	.18	>1.0

(10) Methoxychlor and other compounds vs. Cimex lectularius and Pediculus humanus corporis as contact sprays in white oil (P31) solution applied at rate of 0.36 mg spray/cm^2: 418 419

Insecticide	LC_{50} (% Concentration) For	
	Cimex	Pediculus
Methoxychlor	0.5	0.9
Lindane	.05	.02
p-Chlorophenyl chloromethyl sulfone	.2	.1
DDT	.5	.3
DDD	1.2	.9
DFDT	5.0	1.4

(11) Methoxychlor and other compounds: Speed of toxic action vs. Macrosiphum pisi: 520

Insecticide	Dust Conc. (%)	Temp (°F)	Time (Hrs: Min) To Yield	
			50% Kill	98% Kill
Methoxychlor	10	75	2:1	5:34
Toxaphene®	5	72	13:20	19:1
Chlordane	5	72	9:24	18:8
EPN®	.86	74	5:26	8:6
Dieldrin	1	75	4:7	6:43
Aldrin	1	75	3:44	7:32
DDD	5	72	2:34	4:35

Insecticide	Dust Conc. (%)	Temp (°F)	Time (Hrs: Min) To Yield 50% Kill	Time (Hrs: Min) To Yield 98% Kill
Parathion	1	70	1:8	1:43
"	2	70	1:21	1:53
DDT	5	72	0:57	1:45
Lindane	1	72	0:56	1:54
Rotenone	5	72	0:47	1:23
TEPP	.18	74	0:20	0:56
Nicotine	1	72	0:15	1:12
"	3	72	0:12	0:50
Pure Talc		67-72	13:28	23:51

c) Methoxychlor and beneficial insects:

(1) See, in this work, the section titled Bees and Insecticides.

(2) Toward Apis mellifera the oral and contact toxicity of methoxychlor present a hazard slightly less than DDT; methoxychlor is slightly toxic, comparatively, by these routes. On residual contact methoxychlor is quite highly toxic for bees. 927

(3) Considered as a safe insecticide (for bees) when used on blooming plants under proper conditions. 3099

(4) By others, methoxychlor is placed among those insecticides moderately toxic for bees. 131

d) Pharmacological, pharmacodynamic, physiological, etc.; insects.

(1) The properties of methoxychlor toward insects, for instance, mode of entry, action in the insect body, symptoms of toxicity, etc., resemble closely those of DDT q.v. 3278

(2) Like DDT, methoxychlor has a high lipoid/water partition coefficient; highly effective on the neuraxon sheath. 3278

(3) Like DDT, methoxychlor has toward insects (Musca domestica) a negative temperature coefficient. Mortality among flies exposed to residual deposits at 70°F is greater than among those exposed to identical deposits at 90°F; in this regard methoxychlor stands with DDT, DDD, and in contrast to toxaphene, chlordane, aldrin, dieldrin, parathion. 1561

(4) In methoxychlor poisoned insects (e.g. Blattella germanica injected with a toxic dose) an immediate rise in O_2 consumption is registered (an index of muscular action, excitation, tremor, etc., due to nerve impulse discharge and excitation) without latent period. In Blattella O_2 consumption rose immediately from 0.6 mm^3/minute/insect to ca. 3 mm^3/minute/insect within 0.5 to 1 hr. followed, with the onset of paralysis, by a decline in O_2 uptake, precipitate at first and with a slow steady decline later. 1441 2041 2042

(5) As in the case of other chlorinated hydrocarbons tested, methoxychlor at 10^{-3} M gave complete inhibition (as tested by O_2 uptake in the Warburg apparatus) of a Periplaneta americana coxal muscle cytochrome oxidase preparation; at 10^{-5} M a transient stimulation of O_2 uptake was registered. 2305

(6) Resistance:

(a) In response to selection by exposure, high orders of resistance toward methoxychlor have appeared in Musca domestica biotypes. 373

(b) Rise in resistance (by selection exposure) to DDT on the part of Musca appears to reveal a concomitant rise in methoxychlor resistance. 2098 373

(c) Anomalously methoxychlor, which is less effective than DDT vs. DDT-non R biotypes of Musca is more effective than DDT vs. DDT-R biotypes. 2231

(d) Resistance to methoxychlor ("developed" by exposure selection) for instance in the Methoxy-I biotype (selected against methoxychlor for 21 generations with an 80-fold rise in methoxychlor tolerance) showed no concomitant rise in DDT tolerance. 373

(e) In judging the significance of so-called parallel or concomitant resistance to several insecticides appearing as result of exposure selection against one insecticide, phenomena of "vigor resistance" resulting from intensive selection per se must be weighed against insecticide resistance ad hoc. 1597 2231

(f) For tabular data pertinent to methoxychlor resistance in insects see the section, in this work, titled Resistance. Also note the data, in this present section for various Musca biotypes, in the table of quantitative toxicity of methoxychlor for insects.

e) Field and other experiences reported; control of economic insects by methoxychlor.

(1) Vs. Musca domestica: As a bait in sugar, molasses etc., methoxychlor proved unsatisfactory for fly control in the field at 2% concentration. Only 25% mortality was yielded by methoxychlor at 50 mg/k medium in the case of Musca larvae (maggots) in breeding media. 1915 1326

(2) Vs. Pieris rapae and Trichoplusia ni larvae: At 3% concentrations gave 60.9% control (vs. 88.2% for DDT). 796

(3) Vs. Anticarsia gemmatilis: Far superior to cryolite in control of. 110

(4) Vs. Cirphis unipuncta, Prodenia eridania, Laphygma frugiperda: Inferior to DDT in control of. 1572

(5) Vs. Heliothis armigera: As solutions and emulsions, inferior to DDT in control of. 256

(6) Vs. Argyrotaenia velutinana: Valueless in control of. 1199

(7) Vs. Grapholitha molesta: Slightly inferior to DDT and parathion. 560

(8) Vs. Carpocapsa pomonella: Unsatisfactory in control of. 2379

(9) Vs. Pyrausta nubilalis: Negligible residual effect; inferior to DDT in aircraft sprays. 675,106,735,105

(10) Vs. Pectinophora gossypiella: As effective as DDT; permits aphid pullulation. 91

(11) Vs. Hylemyia brassicae and H. floralis: Ineffective. 796

(12) Vs. Dacus dorsalis: Superior to DDT and DCPM (which are highly effective) in mango protection. 1574

(13) Vs. Epilachna varivestis: Superior to DDT in dusts, but not in aerosols. 323,801

(14) Vs. *Epitrix* sp.: Slightly less toxic than DDT; vs. *E. hirtipennis* sprays gave 90-95% control. 3143,820

(15) Vs. *Ceratoma trifurcata*: Gave complete control of. 801

(16) Vs. *Diabrotica duodecempunctata*: Area treatment, 10% dusts, gave 80% control. 1876

(17) Vs. *Dendroctonus monticolae*: Less effective than BHC in cut log protection. 1854

(18) Vs. *Pantormus leucoloma*: Good control with sprays at 2 lbs/acre. 248

(19) Vs. *Cimex lectularius*: Equal to DDT; superior to other DDT analogs. 419

(20) Vs. *Aëdes* spp (larvae): About equal to DDT; completely effective at 1 lb/acre. 353

(21) Vs. *Anopheles* spp.: As residual spray effectiveness on basis of initial kill and lasting quality: DDT > methoxychlor > methyl-DDT > DDD > DFDT. 2466

(22) Vs. *Simulium venustum* and *S. vittatum* (larvae): Equal to DDT; superior to chlordane, BHC, toxaphene, lindane. 1192

(23) Vs. *Siphona irritans*: Equal to DDT in control of as a cattle suspension spray, and proved fastest acting. 920,1884 2861,788,2183

(24) Vs. *Hypoderma bovis* and *H. lineatum*: Ineffective. 3066

(25) Vs. *Melophagus ovinus*: Complete control of with sprays and dips; effect endured 4 months. 959

f) *Screening data*: Consult Ref. 1801

121

β-METHYLALLYL CHLORIDE (3-Chloro-2-methyl propene-1; 3-Chloro-2-methyl-1-propene; γ-Chloroisobutylene; Isobutenyl chloride.)

$CH_2Cl\text{-}C(CH_3) = CH_2$; $CH_2 = C(CH_3)\text{-}CH_2Cl$ Molecular weight: 90.55

GENERAL

[Refs.: 2618, 2835, 339, 338, 337, 2483, 2485, 3173, 2629, 2630, 697]

An insecticidal fumigant, useful against various stored products insects. Among fumigants methylallyl chloride may be considered to be one of the more recent introductions.

PHYSICAL, CHEMICAL

[Refs.: 2618, 2835]

A colorless liquid of strong, rather pleasant, petroleum-like odor, and slightly irritant; b.p. 71°-72°C; $d_{4°}^{20°}$ 0.925; specific gravity of gas (air = 1) 3.1; bulk density: 490 cc per lb, 7.7 lbs per gallon; forms explosive mixtures with air at 93-375 g per m^3 (5.8-23.4 lb per 1000 ft^3); burns with a smoky flame; the commercial grade, containing 95% β-Methylally chloride with isocrotyl chloride as the chief impurity, is of dark color; there is no significant difference in toxicity to insects of the pure or the commercial product.

TOXICOLOGICAL

1) Toxicity for higher animals: [Refs.: 2835, 3199, 4, 3]

   a) In contrast to its isomer (1-chloro-2-methyl-1-propene) β-methylallyl chloride is the cause of delayed death in low concentrations, presumably because of severe tissue damage. β-Methylallyl chloride is more irritant than its isomer and causes greater increase in the blood pressure of exposed rabbits.

      (1) Mice: Counting deaths over 48 hrs, the MLC (10 minutes exposure) = 0.362 mg/l (4 m M/l); the maximum tolerated concentration = 0.0453 mg/l (0.5 m M/l).

2) Phytotoxicity: 2618

   a) Effects on the germination capacity of wheat, corn:

      (1) No deleterious effect on corn, wheat, of 9.1% or less moisture content at dosages to 1cc per 5 lbs (2.96 gallons per 1000 bushels) which is 13 times the dosage for 95% kills of test insects.

      (2) In grain of moisture content less than 9% there are increasingly severe effects on germinability:

	% Decreased in Germinability		
	At 0.5 cc/5 lb (1.48 gal/1000 bu)	At 1cc/5 lb (2.96 gal/1000 bu)	At 5 cc/5 lb (14.8 gal/1000 bu)
Corn (12.9% moisture)	21	41	8 % still germinable
Wheat (" ")	12	52	No germination.

3) Toxicity for insects:

   a) Quantitative:

      Toxicity of β-methylallyl chloride for 8 species of stored products insects exposed at 70°F for 2 and 6 hrs. in 100 ft^3 empty fumatoria; adult insects: 2005

Insect	LC_{50} (mg/g)		LC_{95} (mg/l)	
	2 Hrs. Exposure	6 Hrs. Exposure	2 Hrs. Exposure	6 Hrs. Exposure
Acanthoscelides obtectus	36	18	58	28
Oryzaephilus surinamensis	43	19	65	29
Rhizopertha dominica	68	25	96	41
Sitophilus granarius	65	25	87	45
Sitophilus oryzae	41	12	58	27
Stegobium paniceum	47	27	77	39
Tribolium confusum	58	27	75	41
Zabrotes pectoralis	14	10	26	18

Insect	Route	Dose	Dosage	Remarks	
Cimex lectularius (older nymphs)	Fumig	LC_{95-100}	25-30 mg/l	Exp. 5 hr., 25°C, 12 l flasks.	2622
Cimex lectularius (adult)	Fumig	LC_{95-100}	<25 mg/l	" " " " " " " .	2622
Cimex lectularius (eggs)	Fumig	LC_{95-100}	<25 mg/l	" " " " " " " .	2622
Oryzaephilus surinamensis	Fumig	LC_{50}	0.0066±.0027 cc/l	Exp. 24 hrs., 30°C, empty vessel.	2618
Tenebrioides mauritanicus (adult)	Fumig	LC_{50}	0.131; 0.108 cc/5 lb	24 hr. exposure at 30°C in containers holding 5 lb lots of shelled whole corn.	2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{50}	0.121; 0.1 g/5 lb		2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{95}	0.208; 0.191 cc/5 lb		2603
Tenebrioides mauritanicus (adult)	Fumig	LC_{95}	0.192; 0.177 g/5 lb		2603
Sitophilus oryzae (adult)	Fumig	LC_{50}	0.0055±.002 cc/l	Exp. 24 hrs, 30°C, empty vessel.	2618
Sitophilus oryzae (adult)	Fumig	LC_{95}	0.0082±.002 cc/l	" " " " " " .	2618
Oryzaephilus surinamensis (adult)	Fumig	LC_{95}	0.0092±.0027 cc/l	" " " " " " .	2618
Tribolium castaneum (adult)	Fumig	LC_{50}	0.0088±.0019 cc/l	" " " " " " .	2618
Tribolium castaneum (adult)	Fumig	LC_{95}	0.0118±.0019 cc/l	" " " " " " .	2618
Tribolium confusum (adult)	Fumig	LC_{50}(ca.) 21 da	12 mg/l	Exp. 5 hrs., 25°C, static fumigation.	2629
Tribolium confusum (adult)	Fumig	LC_{95}(ca.) 21 da	19 mg/l	" " " " " " .	2629

(1) Toxicity for insects exposed 24 hrs, at 30°C in 1 gallon jars containing 5 lbs of shelled whole corn; insects placed at top and at bottom of the grain: 2618

Insect	LC_{50} (cc/5 lb corn)		LC_{95} (cc/5 lbs corn)	
	At Top	At Bottom	At Top	At Bottom
Tribolium castaneum	0.036 ± .011	0.041	0.051 ± .011	0.055
Oryzaephilus surinamensis	0.055 ± .011	0.058	0.068 ± .012	0.073
Sitophilus oryzae	0.025 ± .011;0.054 ± .01	0.030;0.059	0.037 ± .011;0.065±.01	0.045;0.075
Tribolium castaneum	0.038	close to 24 hr. exp.	0.047	close to 24 hr. exp. (exp. 1 wk at 30°C)

(2) Toxicity of methylallyl chloride alone, and in mixture with CCl_4, for Tribolium castaneum and Sitophilus oryzae, exposed in containers with shelled corn: 2618

Fumigant	% v/v Components	Insect	LC_{50} cc/5 lbs Corn	LC_{95} cc/5 lbs Corn
β-Methylallyl chloride	100	T. castaneum	0.039	0.053
" " " "	100	S. oryzae	.042	.056
" " " " + CCl_4	75:25	T. castaneum	.044	.058
" " " " "	75:25	S. oryzae	.039	.051
" " " " "	50:50	T. castaneum	.066	.084
" " " " "	25:75	S. oryzae	.108	.132
" " " " "	16.7:83.3	T. castaneum	.119	.138
" " " " "	16.7:83.3	S. oryzae	.107	.135
CCl_4	100	T. castaneum	.138	.169
"	100	S. oryzae	.166	.232

(3) Fumigation of shelled corn in steel bins: 2618

Fumigant	Gallons per 1000 Bushels	Bin Capacity (Bu)	% Mortality Of			
			T. castaneum	O.surinamensis	S. oryzae	Mean
β-Methylally chloride + CCl_4 9:91	2	2000	83.2	93.0	79.2	87.5
" " " " " "	2	2740	89.7	91.8	93.9	
" " " " 12.5:87.5	2	2000	87.1	94.9	82.5	93.3
" " " " " "	2	2740	94.9	99.2	96.0	
" " " " 16 :84	2	2000	90.3	96.9	90.1	94.0
" " " " " "	2	2740	91.5	97.7	97.2	
CCl_4	1	2000	71.2	87.1	39.4	56.1
"	1	2740	66.5	85.8	55.9	
"	2	2000	88.6	94.7	60.5	74.9
"	2	2740	91.7	92.6	59.2	

(4) 1 lb methylallyl chloride + CCl_4 to make one gallon at the rate of 2 gallons of the mixture per 1000 bushels protected wheat and corn, in steel bins against: Sitophilus oryzae, S. granarius, Rhizopertha dominica, Plodia interpunctella, Sitotraga cereallella, etc. 609

(5) Dosages of β-methylallyl chloride required to yield 50% and 95% mortality of Tribolium confusum and Sitophilus granarius, exposed 24 hrs. at 80°F at various depths in whole wheat grain in 28 l cans, 14.5 inches high, diameter 12.5 inches each containing 30 lbs grain to a depth of 8 inches, with 6.5 inches free space above grain surface: 2009

(a)

Position in Grain (Inches Depth)	T. confusum		S. granarius	
	LC_{50} (mg/l)	LC_{95} (mg/l)	LC_{50} (mg/l)	LC_{95} (mg/l)
At surface	7.2	14.2	6.0	12.0
2 inches	9.0	22.0	8.5	14.0
5.5 inches	11.0	29.5	9.5	15.0

(b) Dosages, in order of effectiveness of various fumigants to yield 95% mortality of Tribolium confusum and Sitophilus granarius at the least effective exposure level in wheat under conditions described above (5.5 inches): 2009

T. confusum

Fumigant	mg/l	cc/0.5 bushel
Methyl bromide	5.3*	0.09
Acrylonitrile	19	.67
Ethylene chlorobromide	28	.46
Methylallyl chloride	29.5	.89
Ethylene oxide	30	.95
1,1-Dichloro-1-nitroethane	30.1	.59
HCN	39	1.6
CS_2	54	1.2

S. granarius

Fumigant	mg/l	cc/0.5 bushel
Methyl bromide	3.9	0.06
Acrylonitrile	6.8	.24
Ethylene oxide	14.3	.45
Methylallyl chloride	15	.45
1,1-Dichloro-1-nitroethane	21.7	.43
Ethylene chlorobromide	39.1	.65
CS_2	43	.95
Ethylene dibromide	60	.77

(b) Dosages, in order of effectiveness of various fumigants to yield 95% mortality of Tribolium confusum and Sitophilus granarius at the least effective exposure level in wheat under conditions described above (5.5 inches): (continued) 2009

T. confusum

Fumigant	mg/l	cc/0.5 bushel
Ethylene dibromide	56	.72
CCl_4	110*	1.9
Ethylene dichloride	111	2.5
Acrylonitrile 50:CCl_4 50	36	.84
Ethylene Cl_2 75:ccL_4 25	59.5	1.25
Eth. chlorobromide 5:CCl_4 95	68.1	1.3
Ethylene Br_2 5:CCl_4 95	70	1.2
Eth. chlorobromide 10:CCl_4 90	77	1.35

S. granarius

Fumigant	mg/l	cc/0.5 bushel
HCN	60.4	2.5
Ethylene dichloride	>200	>4.46
CCl_4	230	4.04
Acrylonitrile 50:CCl_4 50	19	.44
Eth. chlorobromide 10:CCl_4 90	80	1.4
" " 5:CCl_4 95	94	1.65
Ethylene Br_2 5:CCl_4 95	113.9	>2.0
Ethylene Cl_2 75:CCl_4 25	190	4

* = least effective at surface.

For data on the comparative toxicity of β-methylallyl chloride vis-a-vis various other insecticidal fumigants consult, in this work, the tabulations under the general treatment titled, Fumigants.

122

METHYL BROMIDE (Bromomethane; Monobromomethane.)

CH_3Br Molecular weight: 94.95

GENERAL [Refs.: 539, 353, 2815, 1059, 757, 61, 741, 2199, 3199, 2067, 1013, 1944, 1943, 1732, 404, 2144, 2430, 1947, 227, 3200, 2662, 605, 611, 1327, 436, 3261, 341, 487, 2427, 2967, 851, 834, 2324, 364, 2500]

A powerful insecticidal fumigant of wide use which is particularly valuable in low temperature fumigation. Methyl bromide has a high rate of diffusion and penetration into spaces, as well as into sacked and packaged materials. Low solubility in water gives methyl bromide advantage in the fumigation of materials of high moisture content. The substance may be readily and rapidly air-washed and "desorbed" from fumigated materials. It leaves no residual odors, tastes, or stains. Highly toxic to a very wide range of insects, methyl bromide kills pests in all stages of development, including the egg. Methyl bromide may be rapidly volatilized; it is non-inflammable, and non-explosive at insecticidally effective concentrations in air. It lends itself to vault, building, railroad car, ship, soil, domestic, and vacuum fumigation methods. Employed, also, for the control of rodents in buildings, ships and fields. An effective control for certain nematodes. Methyl bromide is widely employed in quarantine fumigation of numerous products, including live nursery stock, bulbs, plants, shrubs, both in bare-root condition and in sacked earth balls; useful in the fumigation of orchids. Methyl bromide is effective against pests and stored products insects of grains in elevators, bins, flour mills, cereal-processing works, sacked and packaged grains and cereal products, dry seeds and legumes, dried fruits, nuts, coffee beans, chocolate, dried vegetables, cheese, candies, dried milk, margarine, etc.; useful also in protection and fumigation of fresh products such as onions, tomatoes, potatoes, dates, artichokes, pears, pineapples, olives, figs, mushrooms. Useful in soil sterilization, delousing fumigation of clothing (shoes, furs excepted), fumigation of carpets, furniture, cotton-picking machines, dairy premises. Effective fumigant of tobacco, cotton-seed meal, and successful in tarpaulin fumigation techniques. Methyl bromide is used under certain circumstances in termite and ant control. Methyl bromide is easily handled and stored, since it is non-inflammable and may be kept in cylinders or canisters as a liquid under its own vapor pressure. Among more recently developed uses is the fumigation of Christmas trees and greens from gypsy moth infested areas to destroy the eggs of that insect. Methyl bromide is also somewhat acaricidal. In addition to insecticidal, nematocidal, and rodenticidal properties methyl bromide is an effective fungicide.

PHYSICAL, CHEMICAL [Refs.: 2231, 61, 3199, 2120, 129, 2221]

A colorless gas at ordinary temperatures; a colorless liquid at low temperatures, or when confined under pressure in containers; non-inflammable and ignitable only by intense electric spark, under which conditions a 14% mixture with air is explosive; freezing point -93.7°C (-135.4°F); $d_{0°}^{0°}$ (liquid) 1.732; specific gravity as a gas (air = 1) 3.2 at 20°C; b.p. 3.5°C (38.3°F); v.p. 1824 mm Hg at 25°C, 760 mm Hg at 4.6°C; vapor saturation at 25°C = 2860 mg/l; very slightly soluble in water (1.34 g/100 cc at 25°C); soluble freely in alcohol, ether, chloroform, carbon disulfide; vapor density 2471 lb/ft³ at 20°C; bulk density 262 cc/lb, 14.4 lb/gal at 0°C; maximum existing as vapor at 68°F in 1000 ft³ = 200 lbs; forms in cold water a dense white precipitate (hydrate); stable; non-corrosive; odor is slight, sweetish, difficult to detect, being insidious and giving no warning; under thermal decomposition (in contact with fire) methyl bromide + air mixtures yield such irritant gases as hydrogen bromide, bromine, carbon oxybromide in addition to CO_2 and CO; in contact with hot metal highly irritant gases may be formed which aggravate the toxic action of CO.

a) Formulations: Available in glass ampoules to 50 cc, 1 lb tins or metal cylinders for direct use; chloropicrin sometimes added as an irritant warning agent; mixed with CO_2 (in proportions to yield maximum insecticidal effectiveness) in 50 lbs steel pressure cylinders. Methyl bromide in cans and containers at room or ordinary temperatures is at considerable pressure; only approved, self-gasketing, and tight openers should be employed in opening containers. Dispensers which measure dosages in lbs are available. Methyl bromide must be handled with care!

TOXICOLOGICAL

1) General remarks:

a) One of the most toxic of the common organic halides, the action is insidious, without warning. Effect of re- 2221
peated exposures is additive and cumulative. A neurotoxic and narcotic agent with a characteristic delayed 3199
action. Damages the nervous system, kidneys, lungs; combines with sulfhydryl group (SH^-) of proteins 61,56,1665
and enzymes. 1356,1983, 851

b) Maximum allowable concentration for continuous exposure = 20 ppm; 3000 ppm in 30-60 minute ex- 2221,1665
posures are dangerous; serious injury follows 1 hour exposure at 2000 ppm; maximum tolerable concen- 353
tration (based on experiences with Guinea pigs) = 3.9 mg/l for 1 hour, 0.19 mg/l for 8 hours.

c) Those fatal and non-fatal human poisonings which are on record have been reviewed and summarized in Ref. 3199.

d) Among 90 human subjects, industrially exposed to concentrations up to 35 ppm, 33 showed mild intoxica- 3240
tion; 22 showed skin lesions.

e) No health hazard is involved by consumption of cereal products fumigated at rate of 1 lb methyl bromide 129
per 1000 ft^3; such treatment is permissible.

f) Soil accumulation presents no health hazard. 129

g) Precautions are essential. Gas masks are to be worn on entering spaces under fumigation; contact of 61
methyl bromide or contaminated clothing with the skin must be avoided since severe burns may follow such exposure. The vapors are to be considered extremely hazardous to all animals.

2) Toxicity for higher animals:

a) Acute toxicity:

Animal	Route	Dose	Dosage (mg/l;ppm)	Remarks	
Rat	inh	LC_{100}	0.63 ; 514	Continuous exposure for 6 hrs. causes death.	1652
Rat	inh	LC_{100}	0.315; 257	" " " 22 hrs. " "	1652
Rat	inh	LC_{100}	10.0 ; 2570	" " " 42 min. causes death.	1652
Rat	inh	LC_{100}	20.0 ; 5140	" " " 24 min. " "	1652
Rat	inh	LC_{100}	50.0 ; 12,850	" " " 6 " " "	1652
Guinea Pig	inh	LC_{100}	— ; 450	" " " 6 hrs. " "	2746
Guinea Pig	inh	LC_{100}	— ; ca. 280	" " " 10 hrs. " "	2746
Rabbit	inh	LC_{100}	0.63 ; 514	" " " 11 hrs. " "	1652
Rabbit	inh	LC_{100}	0.315; 257	" " " 24 hrs. " "	1652
Rabbit	inh	LC_{100}	10.0 ; 2570	" " "132 min. " "	1652
Rabbit	inh	LC_{100}	20.0 ; 5140	" " " 84 min. " "	1652
Rabbit	inh	LC_{100}	50.0 ; 12,850	" " " 30 min. " "	1652
Rat	inh	LC_{50}	21±2 ; 5480	" " " 15 min; death in 2-10 days.	513

b) Sub-acute; repeated exposures:

(1) Guinea pigs tolerated 6 hr. exposures to 200 ppm, 10 hr. exposures to 100 ppm. 3199,2746

(2) Guinea pigs (2) given 15 minute per day exposures to "relatively high concentrations": 1 subject 3199,1194
became "nervous", dead on 5th day, the other survived 11 days, developing hind-leg paresis from which there was recovery before death.

(3) Various animals (rat, monkeys, Guinea pigs) tolerated 7 to 8 hrs. daily exposures to 33 ppm for 3199,1652
"many months" without overt effects; rabbits at 33 ppm showed lung irritation, but tolerated repeated exposure to 16 ppm without overt effects.

3) Pharmacological, pharmacodynamical, physiological, etc.; higher animals:

a) Absorption into body is via lungs, or if taken orally, by the gastrointestinal tract; absorption via 2759,3199,377
the unbroken skin is in question.

b) Metabolic fate:

(1) Partial decomposition with increase in non-volatile Br^- in blood, (rabbit). 3199,1653,2267

(2) Preferential (?) reaction with SH^- yields HBr giving origin to bromides. 3199,1983,1847

(3) Hydrolysis (?) yields bromide + CH_3OH which yields formaldehyde and formic acid. 3199,2267,1042

(4) Wide distribution in body tissues; storage in lipoid rich tissue. 3199, 884,1478

(5) Excretion via lungs, and as bromides in urine. 3199,2267, 549

c) Pathology; (animals): 3199

(1) Pulmonary irritation, circulatory failure; lungs: Hyperaemia, hemorrhage; respiratory tract: Echymoses, various effluvia; heart: Sometimes dilatation, endocardial hemorrhage; viscera: Congestion, particularly of liver, kidney, spleen; brain: Normal to congested or oedematous.

(2) In acute intoxication pulmonary oedema was prime death cause.

(3) In sub-acute, chronic intoxication: Degeneration of heart muscle, liver, kidney, pancreas, gastrointestinal irritation, bronchopneumonia. Neurological symptoms not supported by overt neuropathological changes.

d) Methyl bromide intoxication in man:

(1) A very full treatment may be found in [Refs. 3199, 1356, 3200].

(2) Onset of toxic symptoms is delayed, with latent period of 1/2 to 48 hours after acute exposure. 851

(3) Early symptoms: Malaise, headache, nausea, vomiting, visual disturbances; pulmonary oedema common. 851

(4) Late symptoms: Late after initial symptoms, tremors occur, giving way to violent Jacksonian convulsions continuing until death, primarily from respiratory failure, viz. poor oxygenation of blood due to lung oedema + failure of the respiratory centers of the CNS. 3199 851

(5) Subacute, chronic intoxication: Most symptoms (save frequent skin irritations) stem from CNS, namely, visual, speech, gait, mental process disturbances; complex neurological abnormalities and syndromes may occur, the abnormalities being persistent and sometimes permanently incapacitating. The effects of methyl bromide are not duplicated by sodium bromide. 851

(6) There exists, at present, no specific therapy.

4) Phytotoxicity: [Refs.: 1013, 895, 952, 2624, 1924, 1707, 1788, 2633, 757, 113, 2501, 1654]

a) Symptoms of toxic effect on plants are first evident on growing tips, roots. 2624

(1) Safe at 1 lb per 1000 ft³ for most greenhouse plants, provided roots are protected by well-watered, wet soil.

(2) Non-dormant roses are susceptible to injury at more than 0.25 lb per 1000 ft³. 2624

(3) Ornamental conifers in active spring growth are susceptible, but not dormant winter stock. 1924

(4) Peach trees (nursery stock) are safe at 2 lbs per 1000 ft³ 4 hr. exposure; at higher concentrations tip injury is reported. 1707

(5) Strawberry plants (dormant) tolerated 3 lbs per 1000 ft³ 3 hr. exposure; non-dormant plants undergo severe damage. 1788 2633

(6) Camellias tolerated 3 lbs per 1000 ft³ but some Azalea varieties were injured; the hazard is enhanced by light and increased temperature, and is inversely proportional to the transpiration rate of the plants during the 6 hrs. following treatment. 952

(7) Apple trees, some varieties e.g. Jonathan, McIntosh, Williams are damaged (fruit) at 2.5 lb/1000 ft³. 2501

(8) Harmless to the germination of legume and cereal seeds and to "seed" sweet potatoes up to 160 mg/l concentrations. 1013 895

(9) Fruits: Delays ripening of tomato, papaya; damages oranges, some apples at 2.5 lb per 1000 ft³. Most fruits were damaged by 6 hr. exposures to 3 lb per 1000 ft³. 2501 1654

b) Best results are obtained on greenhouse plants, leafy shrubs, dormant, potted and canned stock, balled and bare root plants at 80°-85°F using 2.5 lbs per 1000 ft³ with an exposure of 4 hrs. For every 10° below 85°F dosage must be increased by 1/2 lb or exposure by 1/2 hour. Temperature should not rise above 90°F during treatment. 61

c) For fresh fruits, vegetables: 2 lbs per 1000 ft³ at 60°-70°F 4-6 hrs. exposures; under 25-27 inch vacuum 2-3 lb per 1000 ft³ at 70°F for 1-1.5 hrs.; applies to olives, tomatoes, celery, potatoes, whole walnuts, apples, pears etc. 61

d) Fruits and vegetables which may be treated with methyl bromide at concentrations lethal to certain major pests; name of fruit or vegetable is followed, in parenthesis, by the pest controlled: 2067

Potatoes (tuber moth), tomatoes (pin worm), pears (codling moth), green beans (Japanese beetle), pears (San José scale), green corn (European corn borer), peaches (peach twig borer), artichokes (plum moth), avocado (latania scale), celery (vegetable weevil), cauliflower (cabbage worm), turnip (seed-corn maggot) sweet potato (sweet potato weevil), persimmon (mealy bug).

e) Herbaceous plants tolerant to vacuum fumigation with methyl bromide at dosages lethal to Pseudococcus maritimus, Rhizoecus terrestris, Tarsonemus pallidus: 2067

Ferns, Begonia rex, Begonia incarnata, Cyclamen, Coleus, pansy, Strelitzia, Musa, cactus (Christmas), strawberry.

f) Palms which may be treated at 2.5 lb per 1000 ft³ (dosage lethal to Rhizoecus terrestris, Diaspis boisduvalli, Aspidiotus cyanophylli, Aspidiotus camelliae): Kentia, Areca, Phoenix. 2067

g) Orchids vary markedly in tolerance both individually and specifically; however, 3 lbs per 1000 ft³ in a 20 inch partial vacuum are lethal to such orchid pests as: Orchidophilus, Diorymerellus, Mordestelinus, various coccids, in 90 minute exposures at 65°F or over. 2067

h) Grain is not damaged at 1 lb per 1000 ft³ and the 12 hrs. exposures necessary for 100% kills of Sitophilus granarius, Sitotraga cerealella, Tribolium confusum, Oryzaephilus spp., Ephestia spp., Plodia spp, etc. 2067

i) Exposure limits of Camellia and azaleas at various temperatures and dosages of methyl bromide with the exposure times necessary for 100% kills of Lepidosaphes camelliae, Fiorinia theae: 952

Temp. (°F)	Dosage (Lbs/1000 ft³)	Exposure Time (Hrs.)		
		For 100% Insect Kill	Limit For Azalea	Limit For Camellia
60°	1.5	4.5	—	—
"	2.0	3.5	7.0	8.0
"	3.0	2.25	3.5	5.0
"	4.0	1.75	3.0	3.5
70°	.5	9.0	—	—

i) Exposure limits of Camellia and azaleas at various temperatures and dosages of methyl bromide with the exposure times necessary for 100% kills of Lepidosaphes camelliae, Fiorinia theae: 952

Temp. (°F)	Dosage (Lbs/1000 ft³)	Exposure Time (Hrs.) For 100% Insect Kill	Limit For Azalea	Limit For Camellia
70°	1.0	4.5	7.0	8.0
"	2.0	2.5	4.5	5.0
"	2.5	2.0	—	—
"	3.0	1.5	3.0	4.0
"	4.0	1.25	2.0	2.5
80°	.5	7.0	14.0	14.0
"	1.0	3.5	6.0	7.0
"	2.0	2.0	3.0	3.5
"	3.0	1.25	2.5	3.0
"	4.0	1.0	1.0	1.0
90°	.5	5.0	10.0	10.0
"	1.0	2.5	3.5	4.0
"	2.0	1.25	2.0	2.5
100°	0.5	4.0	6.0	6.0
"	1.0	2.0	2.5	3.0
"	2.0	1.0	1.5	1.5
110°	0.5	3.0	3.0	3.0
"	1.0	1.5	1.5	2.0
"	2.0	1.0	—	—

5) Toxicity for insects:

a) Quantitative

(1) Toxicity of methyl bromide for 8 species of stored products insects; adult insects exposed at 70°F in 100 ft³ empty fumatoria for 2 and 6 hours:

Insect	2 Hrs. Exposure LC_{50} ←(mg/l)→	LC_{95}	6 Hrs. Exposure LC_{50} ←(mg/l)→	LC_{95}
Acanthoscelides obtectus	9	22	4.2	6.6
Oryzaephilus surinamensis	17	28	4.4	6.8
Rhizopertha dominica	11	19	3.4	5.5
Sitophilus granarius	18.5	27	4.8	6.8
Sitophilus oryzae	9.5	15	3.6	6.1
Stegobium paniceum	15.5	27.5	4.4	6.7
Tribolium confusum	32.5	44	9.2	13.8
Zabrotes pectoralis	10.5	15.5	3.5	6.0

(2) Quantitative data from various sources:

Insect	Route	Dose	Dosage (mg/l)	Remarks	
Acanthoscelides obtectus (adult)	Fumig	LC_{50}	6.1	At 25°C, 5 hrs. exposure, empty vessel fumigation.	2817
Attagenus piceus (larva)	Fumig	LC_{50}	17.5	" " " " " " " "	1263,2817
Attagenus piceus (adult)	Fumig	LC_{50}	9.5	" " " " " " " "	2817
Brachyrinus ligustici	Soil Fumig	DTC*	450 cc/100 ft²	* = Dose to control; MeBr + dichloroethyl ether + H_2O 1:1:1.	1999
Cimex lectularius (egg)	Fumig	LC_{95-100}	<7	At 25°C, 5 hrs. exposure, empty 12 l flasks.	2622
C. lectularius (older nymphs)	Fumig	LC_{95-100}	9	" " " " " " "	2622
C. lectularius (adults)	Fumig	LC_{95-100}	<7	" " " " " " "	2622
Dacus dorsalis (naked egg)	Fumig	LC_{95}	25 (263 g moles/l)	2 hr. exp.; damage to some tropical produce.	1536
D. dorsalis (larva) 3rd instar	Fumig	LC_{95}	19 (200 g moles/l)	" " " " " " " "	1536
D. dorsalis (egg, naked)	Fumig	LC_{50}	15	At 71°-80°F, 2 hrs. exposure, empty vessel fumigation.	255
D. dorsalis (egg, naked)	Fumig	LC_{95}	24.5	" " " " " " " "	255
D. dorsalis (larva, 3rd instar)	Fumig	LC_{50}	9.2	" " " " " " " "	255
D. dorsalis (larva, 3rd instar)	Fumig	LC_{95}	18.5	" " " " " " " "	255
Limonius canus L. californicus	Fumig	LC_{50}	5.9	At 77°F, 5 hrs. exp. in 1 l flasks with 500 g soil.	1958
Oryzaephilus surinamensis (adult)	Fumig	LC_{50}	8.0	At 25°C, 5 hrs. exposure, empty vessel fumigation.	2817
Pantormus spp. (all stages)	Soil Fumig	DTC*	4.7 cc/ft²	* = Dose to control (100% kill) 3.75 day exp., 62°-89°F.	2030
Pantormus spp. (all stages)	Soil Fumig	DTC*	4.7 cc/ft	100% kill; 6 day exposure at 45°-62°F.	2030
Plodia interpunctella (larva)	Fumig	LC_{50}	5.0	At 25°C, 5 hrs. exposure, empty vessel fumigation.	2817,1263
P. interpunctella (adult)	Fumig	LC_{50}	3.1	" " " " " " "	2817,1263
Rhizopertha dominica (adult)	Fumig	LC_{50}	5.4	" " " " " " "	984
Sitophilus granarius (adult)	Fumig	LC_{50}	7.4	" " " " " " "	2816, 156
S. granarius (adult)	Fumig	LC_{99}	8.4	" " " " " " "	2816, 156
S. granarius (adult)	Fumig	LC_{50}	3.8	At 35°C, " " " " "	2817
S. granarius (adult)	Fumig	LC_{50}	4.8	At 30°C, " " " " "	2817
S. granarius (adult)	Fumig	LC_{50}	5.5	At 25°C, " " " " "	2817
S. granarius (adult)	Fumig	LC_{50}	6.5	At 20°C, " " " " "	2817
S. granarius (adult)	Fumig	LC_{50}	7.5	At 15°C, " " " " "	2817
S. granarius (adult)	Fumig	LC_{50}	14.5	At 10°C, " " " " "	2817
S. granarius (adult)	Fumig	LC_{50}	46.0	At 5° C, " " " " "	2817
S. granarius (adult)	Fumig	LC_{50}	70.0	At 0° C, " " " " "	2817
S. granarius (adult)	Fumig	LC_{50}	3.3	At 25°C, " " " " "	2817
Sitophilus oryzae (adult)	Fumig	LC_{50}	4.0	At " " " " " " "	1263,2817

(2) Quantitative data from various sources: (continued)

Insect	Route	Dose	Dosage (mg/l)	Remarks	
S. oryzae(adult)	Fumig	LC_{50}	5-7	At 30°C, 4 hrs. exp., 250-500 cc empty flasks.	47
S. oryzae(adult)	Fumig	LC_{50}	2-3	At 30°C, 24 hrs. " " " " " "	47
Sitophilus oryzae (adult)	Fumig	LC_{50}	4.0	At 25°C, 5 hrs. exp., empty vessel fumigation.	2816, 156
S. oryzae (adult)	Fumig	LC_{99}	6.2	" " " " " " "	2816, 156
Stegobium paniceum (adult)	Fumig	LC_{50}	6.5	" " " " " " "	2817
Tenebrio obscurus (larva)	Fumig	LC_{50}	13.0	" " " " " " "	2817
Tenebrioides mauritanicus (adult)	Fumig	LC_{50}	0.12cc/5lb,0.19g/5lb	MeBr+CCl_4 1:9v/v 30°C, 5 hr. exp., in 5 lb lots shelled corn.	2603
T. mauritanicus (adult)	Fumig	LC_{95}	0.161cc/5lb,0.256g/5lb	" " " " " " " " " " " "	2603
Tineola bisselliella (larva)	Fumig	LC_{50}	7.0	At 25°C, 5 hrs., exp., empty vessel fumigation.	2817,1263
Tribolium castaneum (adult)	Fumig	LC_{50}	6.13	" " " " " " "	1732
T. castaneum (adult)	Fumig	LC_{100}	8.75	" " " " " " "	1732
T. castaneum (adult)	Fumig	LC_{50}	6.1	" 27°C " " " " "	2817
Tribolium confusum (adult)	Fumig	LC_{50}	11-13	At 30°C, 4 hrs. exp., 250-500 cc empty flasks.	47
T. confusum (adult)	Fumig	LC_{50}	11.2	At 25°C, 5 hrs. exp., empty vessel fumigation.	2816,156
T. confusum (adult)	Fumig	LC_{50}ca.	ca.8	" " " ", static fumigation.	2629
T. confusum (adult)	Fumig	LC_{100}ca.	ca.11	" " " " " "	2629
T. confusum (adult)	Fumig	LC_{99}	14.4	" " " " " "	2816,156
T. confusum (adult)	Fumig	LC_{50}	10.2	At 25°C, no absorbent present, empty vessel.	1013
T. confusum (adult)	Fumig	LC_{50}	21.0	" ", in presence of patent flour.	1013
T. confusum (adult)	Fumig	LC_{50}	6.7	At 35°C, 95°F, 5 hrs. exp., empty flask.	2817
T. confusum (adult)	Fumig	LC_{50}	7.9	At 30°C, 86°F, " " " "	2817
T. confusum (adult)	Fumig	LC_{50}	10.2	At 25°C, 77°F, 5 hrs. exp., empty flask.	2817
T. confusum (adult)	Fumig	LC_{50}	14.2	" 20°C, 68°F, " " " "	2817
T. confusum (adult)	Fumig	LC_{50}	18.0	" 15°C, 59°F, " " " "	2817
T. confusum (adult)	Fumig	LC_{50}	33.0	" 10°C, 50°F, " " " "	2817
T. confusum (adult)	Fumig	LC_{50}	32.0	" 5°C, 41°F, " " " "	2817
T. confusum (adult)	Fumig	LC_{50}	25.0	" 0°C, 32°F, " " " "	2817
T. confusum (adult)	Fumig	LC_{50}	32.5	At 25°C, 90 min. exp., empty flask, 760 mm Hg.	1013
T. confusum (adult)	Fumig	LC_{50}	28.2	" " " " " " 480 " "	1013
T. confusum (adult)	Fumig	LC_{50}	21.0	" " " " " " 240 " "	1013
T. confusum (adult)	Fumig	LC_{50}	20.3	" " " " " " 120 " "	1013
T. confusum (adult)	Fumig	LC_{50}	14.0	" " " " " " 30 " "	1013
T. confusum (egg)	Fumig	LC_{50}	5.5-5.9	At 25°C, 5 hrs. exp., empty vessel.	1013
Thermobia domestica	Fumig	LC_{50}	1.65	At 30°C, exposure 5 hrs.	1263
Zabrotes subfasciatus (adult ♂)	Fumig	LC_{50}	4.2	At 25°C, 5 hrs. exp., empty vessel.	2817
Z. subfasciatus (adult ♀)	Fumig	LC_{50}	4.7	" " " " " "	2817

(3) Dosages of methyl bromide required to give 50% and 95% mortalities of Tribolium confusum and Sitophilus granarius, exposed for 24 hrs. at 80°F, at the surface of and at various depths in whole grain wheat in 28 l cans, 14.5 inches high, 12.5 inches in diameter, with wheat 8 inches deep and with 6.5 inches free space above the grain: 2009

Depth In Wheat	Dosage For 50% Kill (mg/l)		Dosage For 95% Kill (mg/l)	
	T. confusum	S. granarius	T. confusum	S. granarius
At surface	4.1	2.3	5.3	3.4
2 inches	3.8	2.4	4.5	3.7
5.5 inches	3.8	2.5	4.2	3.9

Dosages (in order of effectiveness) of methyl bromide and other fumigants required to give 95% kills of Tribolium confusum and Sitophilus granarius, exposed at the least effective level in wheat (5.5 inches) under conditions as above:

Compound	T. confusum		Compound	S. granarius	
	(mg/l)	(cc/0.5 Bushel Wheat)		(mg/l)	(cc/0.5 Bushel Wheat)
Methyl bromide	5.3*	0.09	Methyl bromide	3.9	0.06
Acrylonitrile	19	.67	Acrylonitrile	6.8	.24
Ethylene chlorobromide	28	.46	Ethylene oxide	14.3	.45
Methylallyl chloride	29.5	.89	Methylallyl chloride	15	.45
Ethylene oxide	30	.95	1,1-Dichloro-1-nitroethane	21.7	.43
1,1-Dichloro-1-nitroethane	30.1	.59	Ethylene chlorobromide	39.1	.65
Hydrogen cyanide	39	1.6	CS_2	43	.95
Carbon disulfide	54	1.2	Ethylene dibromide	60	.77
Ethylene dibromide	56	.72	HCN	60.4	2.5
Carbon tetrachloride	110*	1.9	Ethylene dichloride	>200	>4.46
Ethylene dichloride	111	2.5	CCl_4	230*	4.04
Acrylonitrile+CCl_4 1:1	36	.84	Acrylonitrile+CCl_4 1:1	19	.44
Ethylene Cl_2+CCl_4 3:1	59.5	1.25	Eth. chlorobromide+CCl_4 10:90	80	1.4
Eth.chlorobromide+CCl_4 5:95	68.1	1.3	Eth. chlorobromide+CCl_4 5:95	94	1.65
Ethylene Br_2 + CCl_4 5:95	70	1.2	Ethylene Br_2 +CCl_4 5:95	>113.9	>2
Eth.chlorobromide+CCl_4 10:90	77	1.35	Ethylene Cl_2 + CCl_4 3:1	>190	>4

* = Least effective at surface.

(4) Toxicity of methyl bromide for Tribolium confusum, exposed under various conditions in empty flasks, and in presence of various sorptive substances; exposure 90 minutes at 25°C: 1013

	LC_{50} (mg/l) At				
	760 mm Hg	480 mm Hg	240 mm Hg	120 mm Hg	30 mm Hg
Empty Flask	32.5	28.2	21.0	20.3	14.0*
" " corrected	26.5	23.0	17.0	16.6	11.4
Raisins	28.1	—	16.8	—	12.2
Wheat Grain	30.4	26.3	17.2	—	14.2
Wheat Flour	50.0	41.9	34.0	32.9	26.0

* Dry vacuum; 10 mg/l = LC_{50} in presence of moisture.

(5) Mortality of Cimex lectularius, exposed under various conditions to methyl bromide for 5 hrs., at 77°F, 760 mm Hg, methyl bromide dosage: 20 mg/l: 2622

	% Mortality Of Cimex Wrapped In		
	Cotton Batting	Woolen Blanket	Woolen Blanket In Barracks Bag
Cimex (older nymphs)	100	100	100
" (adults)	100	100	100
" (eggs)	100	100	100

(6) Exposures necessary (hrs : minutes) to yield 50% and 100% mortalities of Tribolium castaneum adults exposed to 8.75 mg/l methyl bromide alone and with various proportions of CO_2* in the gas mixture: 1732

% CO_2 In Gas Mixture	Methyl Bromide 8.75 mg/l	
	Time For 50% Kills	Time For 100% Kills
0	3 : 40	5 : 00
1.0	3 : 10	4 : 30
5.0	2 : 25	4 : 00
10.0	2 : 05	3 : 00
20.0	1 : 40	3 : 00
40.0	1 : 50	3 : 00
60.0	2 : 20	3 : 30
80.0	2 : 25	4 : 00
99.8	3 : 10	4 : 30

* Maximum insecticidal effect of methyl bromide vs. T. castaneum is manifested with 10% (ca.) CO_2 in the gas mixture.

(7) Effect of methyl bromide vs. Aspidiotus perniciosus (San José scale) when used in fumigation of nursery stock: 222

(I) Concentration Methyl Bromide (g/m^3)	(II) Fumigation Time (Hrs.)	I × II	% Kill
25	0.1	2.5	60.7
25	0.2	5	49.7
25	0.3	7.5	97.6
25	0.4	10	99.6
25	0.8	20	99.0
25	1.0	25	100
25	1.2	30	100

(8) Degree of control (as % mortality) of various insects on various plants, plant products, fruits, etc., exposed for 90 minutes and 30 minutes to methyl bromide: 2068

Insect	Stage	On	°F	Vacuum (inches)	Dosage (lbs/1000ft³)	Exposure (Min.)	% Control
Aspidiotus cyanophylli	1st-3rd	Areca palm	80	20	2.5	90	100
A. lataniae	" "	" "	80	20	2.5	90	100
Carpocapsa pomonella	Larva	lug boxes	85	27	2.5	90	100
" "	Pupa	" "	85	27	2.5	90	100
Chrysomphalus aonidium	Adult	Kentia palm	90	27	1.75	90	100
" "	1st-3rd	Areca palm	80	20	2.5	90	100
Diaspis boisduvalli	1st-3rd	" "	80	20	2.5	90	100
Gnorimoschema lycopersicella	Larva	Tomatoes	97	20	2.5	90	100
G. operculella	Egg	Potatoes	76	20	1.75	90	100
" "	Larva	"	88	20	2.5	90	100
" "	"	"	88	20	2.5	30	97
" "	"	"	89	20	1.75	90	100
" "	"	"	89	20	1.75	30	84

(8) Degree of control (as % mortality) of various insects on various plants, plant products, fruits, etc., exposed for 90 minutes and 30 minutes to methyl bromide: (continued) 2068

Insect	Stage	On	°F	Vacuum (inches)	Dosage (lbs/1000 ft^3)	Exposure (Min.)	% Control
G. operculella	Pupa	Potatoes	75	27	2.5	90	100
Lepidosaphes gloverii	Adult ♀♀	Oranges	53	20	2.5	90	70
Paratetranychus ilicis	Egg	Plane leaves	76	20	2.5	90	100
" "	Adult	" "	76	20	2.5	90	100
Rhizoecus terrestris	"	Palms	88	27	2.5	90	100
Sitophilus granarius	"	Barley	95	27	2.5	90	100
Tribolium confusum	"	Barley	95	27	2.5	90	100

(9) Methyl bromide in control of Popillia japonica (adult) in loaded freight cars: 823

Dosage (Lbs/Car)	°F	% Kill After 24 Hrs.	Final Kill (%)	Exposure (Hrs.)	Days Until 100% Kill
3.5	81-84	97.5	100	2	5
3.75	79.5-86	100	—	2	1
3.75	79.0-81	100	—	2	1
3.75	74-79	100	—	2	1
4.0	79-84	100	—	2	1
4.0	72	100	—	2	1
4.0	73	99.2	100	2	5

In fumigation vaults 100% kills are achieved with 2 lbs/1000 ft^3 at 65°-90°F, 1 lb/1000 ft^3 at 76°-89°F and 0.75 lb/1000 ft^3 at 77°-86°F.

(10) Recommended doses of methyl bromide in fumigation of nursery stock to destroy Grapholitha molesta (Oriental fruit moth) eggs, larvae, adults: 1707

3 lbs/1000 ft^3, exposures of 4 hrs. at 60°F	adults
2 lbs/1000 ft^3, exposures of 4 hrs. at 70°F	
1.5 lbs/1000 ft^3, exposures of 4 hrs. at 60°F	overwintering larvae, eggs.
1.0 lb/1000 ft^3, exposures of 4 hrs. at 70°F	

Based on experiments done at 4 hr. exposures, 760 mm Hg on large numbers per test (100-1000) of eggs, larvae, adults at dosages of 0.5-4.0 lbs per 1000 ft^3.

6) Comparative toxicity of methyl bromide and other fumigants:

a) Tabulations indicating the comparative toxicity of methyl bromide may be found in the general treatment, in this work, titled, Fumigants.

7) Pharmacological, pharmacodynamic, physiological, etc.; insects:

a) Considered to release acid in the tissues of insects and to act as an "irritant poison." 2537

(1) Does not induce narcosis in insects; insects exposed for 5 hours to toxic concentrations appear fully active; death is delayed, following in ca. 48 hours. The delayed effect is marked with Cimex. 2817 2067

(2) Reported to act as oxidant of SH$^-$ (sulfhydryl) containing compounds for example SH$^-$ containing enzymes such as succinic dehydrogenase. 1983

(3) Methyl bromide appears to have no effect on cytochrome oxidase. 1983

b) Susceptibility and resistance to methyl bromide:

(1) In the case of Tribolium the egg is more susceptible than the adult. 3013

(2) Some insect forms, such as Thysanoptera and Coccids, (in the egg stage) are markedly resistant to toxic action of methyl bromide.

(3) Some forms are especially susceptible for instance Carpocapsa pomonella larvae deep in their burrows in pears may be killed at dosages of 0.5 lb per 1000 ft^3 and Aspidiotus perniciosus is killed by 0.25 lb per 1000 ft^3 in 16 hour exposures; Cimex, also, is highly susceptible, complete kills being given by 1 lb per 1000 ft^3. 2067

(4) Particularly methyl bromide resistant biotypes have been reported among the scale insects, for example Aonidiella aurantii, Saissetia oleae, Coccus pseudomagnoliarum and referred to as resistant strains. HCN resistant strains of Anoidiella aurantii are reported to show resistance, likewise, to methyl bromide fumigation as follows: 2560 3395

Susceptibility to methyl bromide of HCN-R, HCN-non R strains of Aonidiella aurantii; exposures of 40 minutes: 3395

Stage	Methyl bromide			HCN		
	Conc. (mg/l)	% Mortality		Conc. (mg/l)	% Mortality	
		HCN-R	HCN-nonR		HCN-R	HCN-nonR
Second Moult	30	96.2	95.2	0.6	14.6	98.9
Early Gray Adult	80	96.1	83.0	0.59	41.1	99.6
Mature ♀	55	77.0	94.4	0.48	54.9	98.6

(5) Of the common materials methyl bromide is the best louse ovicide used at 1 lb per 100 ft^3 for 30 minutes at 760 mm Hg or 15 minutes in a 28 inch vacuum for clothing fumigation. 2992

8) Economic control of insects with methyl bromide: [Refs.: 61, 222, 1662, 3172, 2226, 2324, 364, 2500]

a) At 1-1.5 lb per 1000 ft^3, 15-24 hrs. exposure, 60°-70°F, controls on grains, seeds, legumes and coffee beans in bins, bags, elevators or under tarpaulin: Granary weevil, flour beetles, rice weevil, pea weevil, saw-toothed grain beetle, mites, bean weevil, coffee-bean weevil, Indian meal moth, grain borers, cadelle beetle.

b) In vault fumigation of grain and seeds at 60°F or over, 3 lbs per 1000 ft^3 for 4 hours, 2 lbs for 8 hours, 1 lb for 12 hours controls the insects mentioned in (1).

c) At 1-2 lbs per 1000 ft^3, exposure 12-24 hrs. at 70°F on dried fruits in bulk (boxes, trays, sacks) controls dried fruit beetle, Indian meal moth, raisin moth, saw-toothed grain beetle. Packaged dried fruits (cellophane bags, boxes, cartons) are best treated by vacuum fumigation (25-27 inches vacuum) at 2-3 lbs per 1000 ft^3, exposures 1.5-3 hrs.

d) At 2 lbs per 1000 ft^3, 4-6 hrs. exposure at 60°-70°F or at 2-3 lbs per 1000 ft^3 at 25-27 inches vacuum, 70°F, for 1-1.5 hrs. the following are controlled on fresh vegetables and fruits: Japanese beetle, white fringe beetle, oriental fruit moth, olive scale, tuber moth, sweet potato weevil, pin worm, golden nematode, vegetable weevil, codling moth, mealy bug, plume moth, leaf miner, earwigs, spider mites.

e) At 1-1.5 lbs per 1000 ft^3 15-24 hrs. exposure at 60°F or above, or at 25-27 inches vacuum at 2-3 lbs per 1000 ft^3 for 1.5-3 hrs. at 70°F or over, the following are controlled in packaged flour, cereals, spices, chocolate, nuts, etc. (for oily nuts the lower dosages and times are used to prevent darkening): Indian meal moth, saw-toothed grain beetle, confused flour beetle, red flour beetle, Cadelle beetle, mites, grain moths and dried fruit beetle. In vaults, coarse cereals, rice, whole spices and similar large particle packaged products require at 60°F, per 1000 ft^3: 3 lbs for 4 hrs. 2 lbs for 8 hrs., 1 lb for 12 hrs. Packaged flour, powdered milk, ground spices and ground cereals in vaults at 60°F or over, require per 1000 ft^3: 2 lbs for 12 hrs., 1.5 lbs for 18 hrs., 1 lb for 24 hrs.

f) At 2 1/2 lbs per 1000 ft^3 at 80°-85°F, 2 hrs. exposures at 75% relative humidity the following are controlled on greenhouse plants, shrubs, dormant nursery stock, potted, canned, balled and bare root plants: Leaf miner, scale insects, earwigs, spider mites, mealy bugs, snails, aphids, thrips, weevils and bulb flies. Under 15-27 inches vacuum, 3 lbs per 1000 ft^3 for 1-1.5 hrs. at 60° or more, the above pests on nursery stock, etc., may be controlled also.

g) On rugs, furniture and clothing at 1-1.5 lb per 1000 ft^3, 12-24 hrs. exposures at 60°-70°F, the following may be controlled: Carpet beetles, clothes moths, silverfish, fleas, roaches. Furs, feathers, leather and rubber articles should not be fumigated with methyl bromide.

9) Miscellaneous:

a) Baking tests with flour fumigated at 2 lbs per 1000 ft^3 indicate no change in baking qualities. On sorption there is reaction with wheat flour proteins, with large residues found in the glutenin fraction. Methylation of protein acid groups is suggested as one mode of decomposition of sorbed methyl bromide. 3339

123

METHYLENE CHLORIDE (Dichloromethane; Methylene bichloride.)

CH_2Cl_2 Molecular weight: 84.89

GENERAL

A minor insecticidal fumigant.

PHYSICAL, CHEMICAL

A colorless liquid; freezing point -96.7°C; b.p. 40.2°C; $d^{15^\circ}_{4^\circ}$ 1.335; $n^{15^\circ}_D$ 1.3348; v.p. 415 mm Hg at 25°C; 1.15 parts soluble in 100 parts water at 20°C; miscible with acetone, alcohol, ether; not flammable; not explosive in air; decomposed by contact with open fires and hot iron surfaces; chemically more stable than methyl chloride. 3199

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Although one of the least toxic of chlorinated hydrocarbons, methylene chloride should not be used in small enclosures without adequate protection; 500 ppm = maximum permissible concentration for man. 1487 56

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rabbit	or	LD	1896		1071
Rabbit	sc	MLD	2700	Death within 24 hours.	195
Dog	or	MLD	3000		195
Dog	iv	MLD	200	Death in 30 minutes.	195
Mouse	inh	LC_{50}	56.23 ± .34 mg/l (16,189 ppm)	Exposure 7 hrs.	3024
Mouse	inh	LC	63 mg/l (17,144 ppm)		2315
Mouse	inh	LC	50 mg/l (14,400 ppm)		1938

(1) Guinea Pigs: At 0.8-1.0% in air showed primary irritation followed by depression, tremors, dyspnoea; at 2.0-2.4% the preceding symptoms more marked; at 5.0-5.4%: Marked irritation, progressive depression, narcosis; death after 1-1.5 hours exposure. Recovery followed 2 hour exposures at 2.0-2.4% in air. 2390

(2) Dogs, Rabbits, Guinea Pigs, Rats: Exposures of 7 hours per day, 5 days per week over 6 months at 5000 ppm: No overt effects, save retard in growth of Guinea pigs; no renal irritation, no hepatic injury. 1487

(3) Rats: 30 minute exposures to 5000 ppm: Marked diminution of running activity without other overt depressant effects. 1494

(4) Monkeys, Rabbits, Rats: Exposures to 10,000 ppm for 4 hours per day during 7.5 weeks: No evidence of liver damage in monkeys, rabbits, rats; dogs after 6 exposures: Slight to moderate fatty liver degeneration; liver damage in Guinea pigs also. Slight to moderate narcosis in all; some deaths with lung oedema, congestion. 1494

(5) Rabbits: Repeated dermal application: Hyperaemia followed by scaly desquamation. 1487

(6) Man: In non-fatal intoxications the following symptoms have been noted: Headache, giddiness, stupor irritability, numbness, tingling of limbs; exposures at 8.1 mg/l (2,330 ppm) yielded vertigo in 10 minutes; 30 minute exposures at 4 mg/l (1150 ppm) gave no overt effects. 1.1 mg/l (320 ppm) is just detectable by odor, 4 mg/l produce marked odor. 570 1963

2) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:
   a) Dogs: 3202

(1) At 15,000 ppm in air: Moderate medullary depression, reduction of heart rate and arterial pressure; moderate decrease in respiratory rate; corneal, pupillary reflexes negative in 10-20 minutes; muscular relaxation complete at 25-35 minutes (33-42 mg/100 cc blood).

(2) At 20,000 ppm in air: Reduction in blood pressure twice as marked as in preceding; evidence of myocardial injury; respiratory responses as in preceding; at 15,000-20,000 ppm: Occasional tremors, running movements, twitching, convulsive contraction of diaphragm; onset of narcosis more rapid than at 15,000 ppm.

(3) At 40,000 ppm in air: CNS depression prompt; fall in blood pressure rapid and abrupt with marked medullary depression and progressive heart failure due to injury (primary cause of death); primary respiratory stimulation less marked and subsequent depression more severe with final progressive depression giving way to paralysis; pupillary and corneal reflexes negative in 5 minutes; muscular relaxation complete in 16 minutes (46-50 mg/100 cc blood); marked tremor, twitching, running movement, diaphragm convulsion.

   b) Rabbits: By mouth 1.18 cc/k gave semi-sleep, light narcosis; 1.6 cc/k gave narcosis and death after 29 hours. 1070

c) Reported to be 3.5 times less effective than chloroform as a narcotic; primary excitement, salivation and motor activity during narcosis. Narcosis is preceded by a relatively long excitement phase. Cats and rabbits exposed to 6-7 mg/l: CNS depression, moderate decrease in temperature. 2315 1963

d) Stated to increase cardiac action which declines only shortly prior to death; primary rise, with later fall, in blood pressure. Reported less toxic than chloroform to the heart. Minimum fatal concentration for isolated frog heart variously reported as 0.0465 mol/l, 0.0435 mol/l, 0.016 mol/l and thus less toxic than chloroform (reported variously as 0.007,0.0224 mol/l). 2436 926 3401 1787,1071

3) Toxicity for insects:

a) For Tribolium confusum (adult) exposed for 5 hrs. at 25°C in empty fumigation vessels: LC_{50} = 82 mg/l; LC_{99} = 182 mg/l. 156

b) For Sitophilus granarius (adult) exposed for 5 hrs. at 25°C, empty vessel fumigation: LC_{50} = 380 mg/l. 984

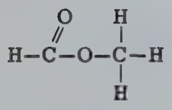
c) For comparison:

	Tribolium confusum		Sitophilus granarius	
	LC_{50} (mg/l)	LC_{99}	LC_{50} (mg/l)	LC_{99}
Acetyl chloride	3.6	5.6	—	—
Propionyl chloride	4.1	8.3	5.0	14.0
Thionyl chloride	2.0	3.8	3.0	9.0

4) For comparative toxicity of methylene chloride and others see, in this work, the general treatment titled Fumigants.

124

METHYL FORMATE


$$H-\overset{\overset{O}{\|}}{C}-O-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-H$$

Molecular weight: 60.05

GENERAL

[Refs.: 669, 1732, 2839, 539, 353, 2815, 757, 1059, 2352, 612, 2670, 1731]

An insecticidal fumigant. The simple, volatile esters (of which the present compound is one) are powerful fumigants for insects. Methyl acetate and methyl propionate, for example, are highly toxic for the scale insect, Aonidiella aurantii. Ethyl formate (as well as methyl formate) is an effective fumigant for individual packages of dried fruits. The maximum insecticidal effect of methyl formate against some insects is shown when the fumigant is mixed with 40% carbon dioxide. Useful as a louse fumigant for infested clothing.

PHYSICAL, CHEMICAL

A colorless, highly inflammable liquid of pleasant odor; lower limit of flammability in air = 5% v/v; must be diluted with CO_2 to reduce the fire hazard; freezing point ca.-100°C; b.p. 31.5°C; $d_{15°}^{15°}$ 0.987; $n_D^{20°}$ 1.344; v.p. 580 mm Hg at 25°C; soluble in water to 1 part to 3.3 parts; miscible with alcohol and similar organic solvents; maximum amount (lbs per 1000 ft^3) which can exist in vapor form at various temperatures:

Temperature (°F)	V. P. (mm Hg)		Lbs As Vapor/1000 ft^3	
	Methyl formate	Ethyl formate	Methyl formate	Ethyl formate
32	241	64	53	17
59	431	164	90	42
68	516	207	106	52
77	614	255	124	62
86	725	312	144	75
95	760	382	148	92
104	760	462	146	109
113	760	558	144	130
122	760	668	142	153

TOXICOLOGICAL

1) A very poisonous vapor for man and animals. The maximum tolerable concentration for 60 minute exposure = 10.9 mg/l, for 8 hour exposure = 3.3 mg/l (based on experiments with Guinea pigs); probable safe concentration for indefinite exposure = 3.7 mg/l (1500 ppm). 1665

2) Exposure to 1% for 2.5 hours, or 5% for 0.5 hour, is lethal. 353

Animal	Route	Dose	Dosage (mg/l)	Remarks	
Guinea Pig	inh	LC	122.7 (50,000 ppm)	Death in 20-30 minutes.	2781

3) Inhalation of methyl formate causes irritation of nasal membranes and conjunctivae; retching and narcosis with death as a result of extreme pulmonary irritation. Considered primarily an irritant lung poison. 2781 1665

a) Moderately hazardous; irritant properties render methyl formate self-warning. Guinea pigs tolerated 1500 ppm for several hours without serious effects; the danger level for 30-60 minute exposure = 15,000 ppm. 1665

4) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Dacus dorsalis (naked egg)	Fumig	LC_{50}	65 mg/l	Exposure 2 hrs., 71-80°F, empty vessel.	255
Limonius californicus (larva)	Fumig	LC_{50}	12.5 mg/l	Relative toxicity (CS_2 = 1) = 2.5	1957
Limonius californicus (larva)	Fumig	LC_{100}	23.0 mg/l	Empty vessel fumigation.	1957
Limonius californicus (larva)	Fumig	LC_{50}	173.7 mg/l	Exposure 5 hrs, 77°F in flasks containing soil.	1958
Limonius canus (larva)					1958
Sitophilus granarius (adult)	Fumig	LC_{50}	20.0 mg/l	Exp. 5 hrs., 25°C, empty vessel fumigation.	2816, 156
Sitophilus granarius (adult)	Fumig	LC_{99}	36.0 mg/l	Exp. 5 hrs., 25°C, empty vessel fumigation	2816, 156
Tribolium castaneum (adult)	Fumig	LC_{50}	17.81 mg/l	Exp. 5 hrs., 25°C; methyl bromide LC_{50} = 6.13 mg/l.	1732
Tribolium castaneum (adult)	Fumig	LC_{100}	25.0 mg/l	Exp. 5 hrs., 25°C; methyl bromide LC_{100} = 8.75 mg/l.	1732
Tribolium confusum (adult)	Fumig	LC_{50}	23.5 mg/l	Exp. 5 hrs., 25°C; empty vessel fumigation.	2816, 156
Tribolium confusum (adult)	Fumig	LC_{99}	37.5 mg/l	Exp. 5 hrs., 25°C; empty vessel fumigation.	2816, 156
Tribolium confusum (adult)	Fumig	LC_{50}	18.0 mg/l	At 25°C, empty vessel, no absorbent present.	1013
Tribolium confusum (adult)	Fumig	LC_{50}	78.0 mg/l	At 25°C, in presence of flour [absorption ratio = 4].	1013

a) Toxicity of several aliphatic esters for Sitophilus granarius (adult): 984

Alkyl Ester	LC_{50} (mg/l)	
	Formate	Acetate
Methyl	15	84
Ethyl	35	56
Propyl	28	45
Isopropyl	34	90

(1) Vs. Limonius spp. methyl formate is the most effective, octyl formate the least effective. 984

(2) Vs. Sitophilus methyl formate is outstanding, but vs. Aonidiella less toxic than either methyl acetate or methyl propionate. 984

(3) Of all the alkyl esters, allyl formate is the most effective vs. Limonius. 1958

b) Comparative toxicity of 4 alkyl esters for Tribolium confusum and Sitophilus granarius adults, exposed for 5 hours at 25°C in empty vessel fumigation: 2816 156

Fumigant	T. confusum (mg/l)		S. granarius (mg/l)	
	LC_{50}	LC_{99}	LC_{50}	LC_{99}
Methyl formate	23.5	37.5	20.0	36.0
Ethyl formate	24.5	32.5	29.0	49.0
Methyl acetate	82.0	130.0	88.0	129.0
Ethyl acetate	83.0	123.0	86.0	178.0

c) Time (in hours) required to give 50% and 100% mortality of Tribolium confusum adults with various mixtures of CO_2 and sublethal amounts of methyl formate: 1731

$\%CO_2$	CO_2 (Alone) Hrs. For		CO_2 + 5 mg Methyl formate/l Hrs. For		CO_2 + 10 mg Methyl formate/l Hrs. For	
	50% Kill	100% Kill	50% Kill	100% Kill	50% Kill	100%Kill
100	6.3	10	1.8	4.0	—	—
75	12.9	20	2.4	6.0	—	—
50	27.7	44	3.6	8.0	1.8	4.0
Larvae					1.5	2.5 - 3.0
Eggs					ca.2-3	6 - 7

d) Exposure time (hours : minutes) required for 50% and 100% mortalities of Tribolium castaneum with various amounts of CO_2 in the gas mixture and methyl formate constant at 25 mg/l: 1732

% CO_2 In Gas Mixture	Methyl Formate Constant At 25 mg/l	
	Time For 50% Kill	Time For 100% Kill
0.0	2 : 30	5 : 00
1.0	2 : 05	3 : 30
5.0	0 : 45	2 : 30
10.0	0 : 25	2 : 00

d) Exposure time (hours : minutes) required for 50% and 100% mortalities of Tribolium castaneum with various amounts of CO_2 in the gas mixture and methyl formate constant at 25 mg/l: (continued)

% CO_2 In Gas Mixture	Methyl Formate Constant At 25 mg/l	
	Time For 50% Kill	Time For 100% Kill
20.0	0 : 19	1 : 30
40.0	0 : 17	0 : 45
60.0	0 : 17	0 : 45
80.0	0 : 17	0 : 45
99.8	0 : 17	0 : 45

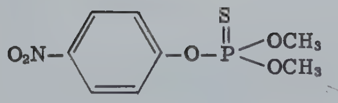
(1) Maximum insecticidal effect of methyl formate was manifested in presence of 40% CO_2 in the fumigant mixture.

5) For data on the comparative toxicity of methyl formate and other fumigants consult the tabulations in the section of this work titled, Fumigants.

125

METHYL PARATHION

(O,O-Dimethyl O-p-nitrophenyl thionophosphate; O,O-Dimethyl O-p-nitrophenyl thiophosphate; O,O-Dimethyl O-p-nitrophenyl phosphorothioate; Dimethyl parathion; E-605; Methyl analogue of parathion; Methyl homologue of parathion.) Metacide®: A proprietary mixture of methyl parathion 24.5%, parathion 6.2%, emulsifier 66.6%.)



Molecular weight: 263.3

GENERAL

[Refs.: 353, 2231, 1458, 2244, 2773, 2247, 2121, 1358, 129, 2120, 861, 1169, 1783, 1787, 3365, 1801]

An insecticide of the general class known as organic phosphate or "organophosphorus" insecticides. Closely related to parathion (O,O-diethyl O-p-nitrophenyl thionophosphate q.v.). Closely resembles parathion in its chemical and toxicological properties and is comparable to it in insecticidal activity. Especially effective against aphids, boll weevil and acarines. Reported to be 10 times as toxic as parathion for Sitophilus granarius and twice as toxic as parathion for Apis mellifera. The toxic hazard for mammals is claimed to be less than in the case of parathion. As Metacide® pronounced especially effective in the orchard control of Carpocapsa pomonella (eggs, young larvae in fruit, adults) although being subject to too rapid weathering.

PHYSICAL, CHEMICAL

[Refs.: 1784, 1339, 2121, 2247, 2231, 129, 2120]

Pure: A white crystalline solid; technical: A tan to brown liquid crystallizing at 29°C; m.p. (pure) 35°-36°C; $d_4^{20°}$ 1.358; $n_D^{35°}$ 1.5515; v.p. 0.5 mm Hg at 109°C (parathion 0.05 mm Hg at 113°C); volatility at 20°C: 0.14 mg/m^3 (parathion 0.09 mg/m^3); very slight solubility in water (ca. 50 ppm at 25°C) and in heptane; slightly soluble in paraffin hydrocarbons; soluble in most aromatic solvents; odor: Pungent, garlic-like; little or no corrosive action; stable for several days in neutral aqueous suspensions; rapidly hydrolyzed in alkaline media at a rate 4.3 times greater than parathion, $K = 9.25 \times 10^{-2}$ min.$^{-1}$ at 15°C; at 150°C isomerization is more than 90% complete in 6 hours; isomerizes more readily than parathion; compatible with lead arsenate, rotenone, pyrethrum, nicotine sulfate, summer and dormant oils, DDT, BHC, chlordane, toxaphene, quinones, fixed coppers, wettable sulfur, dithiocarbamates; questionable compatibility with zinc arsenate, calcium arsenate, Paris green; incompatible with Bordeaux mixture, lime, lime-sulfur;

a) Formulations: Spray, aerosol and dust formulations, and with parathion at 4 to 1 as Metacide®.

TOXICOLOGICAL

1) Toxicity for higher animals: (An impurity of the technical product is more toxic than methyl parathion *per se*)

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	14-42		2231
Rat	or	LD_{50} ca.	15.2		1951
Rat	or	LD_{50} ca.	9-25		129
Mouse	or	LD_{50}	100-200		2247
Mouse	sc	LD	50-100		2773
Rabbit	or	LD	1270	Pure substance, given as such.	746
Rabbit	or	LD	420	Pure substance in corn oil solution.	746
Rabbit	ct	LD_{50}	300-400	As a single, acute exposure.	1951
Rat	ip	LD_{50}	3.5	As Metacide®.	861, 713
Rat	or	LD_{50}	12.7	As Metacide®.	863

a) Chronic toxicity: 129

(1) Sub-lethal doses lower the choline esterase activity; recovery of Ch E activity on termination of exposure.

2) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:

a) Consult, in this work, the general treatment titled, Organic Phosphates.

b) Toxic by all portals of entry: Mouth, skin, respiratory tract; highly hazardous via the eye. 1458

c) The symptoms of poisoning are those of cholinergic intoxication. 1458

(1) In the pure form almost inactive *in vitro* as an inhibitor of choline esterase. 2247,794,797

(2) Converted in the animal body to an active choline esterase inhibitor. 2231

d) Comparison of the intraperitoneal toxicity for rats and the *in vivo* choline esterase inhibition activity of methyl parathion and others: 713

Compound	LD_{50} (mg/k) ip	ID_{50} For Choline esterase *In Vivo* Molar Concentration
Methyl parathion (Metacide®)	3.5	1×10^{-4}
Parathion	5.5	1.2×10^{-6}
Potasan®	15.0	5×10^{-9}
Malathion (tech.)	750.0	1×10^{-4}
Systox	3.0	5×10^{-7}

e) Comparison of the inhibition of erythrocyte choline esterase by methyl parathion and other compounds administered *in vivo*, and incubated *in vitro* with blood of the rabbit: 1288 30

Dose (mg/k)	Compound	Route	Time After Injection Or Incubation (Min.)	% Inhibition Of Choline esterase	
				In Vitro	*In Vivo*
10	Methyl parathion	iv	10	—	67
10	" "	iv	40	8	64
15	" "	iv	10	6	80
15	" "	iv	40	5	65
10	Parathion	iv	10	8	83
10	"	ip	11	9	66
10	"	ip	40	20	81
15	Potasan®	iv	20	26	94
15	"	iv	30	—	97
15	Diisopropyl parathion	iv	10	21	34

3) Residues; residue hazard:

a) Residues generally decline to below 1 ppm in 7 to 21 days after application at normal insecticidal dosage levels; in the soil residue levels drop to below 1 ppm in 4 to 6 weeks. 129

b) Crops should not be harvested for 15 to 30 days after the final treatment with methyl parathion. 129

c) On apple foliage with an initial residue level of 40 ppm, 2 ppm were present in 14 days after treatment; half-life: 3 days. 1298 957

4) Phytotoxicity:

a) At recommended dosages, under proper procedures and conditions, the phytotoxic hazard is reported to be slight. 129

5) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Anopheles quadrimaculatus (4th instar)	Medium	MLC_{100} 48 hr	0.005 ppm	67% kill at 0.0025 ppm.	1766
Apis mellifera (adult worker)	Topical	LD_{50}	1.7 μg/g	LD_{50} parathion = 1.47; 3.5 μg/g.	2231
Locusta migratoria migratorioides (adult)	Topical	LD_{50} 96 hr	0.94 ± 0.1 μg/insect	In tractor oil-cyclohexanone 9:1.	1585
L. migratoria migratorioides (adult)	Topical	LD_{50} 96 hr	0.89 μg/g	In tractor oil-cyclohexanone 9:1.	1585
L. migratoria migratorioides (adult)	Topical	LD_{95}	2.3 ± 0.52 μg/insect	In tractor oil-cyclohexanone 9:1.	1585
L. migratoria migratorioides (adult)	Topical	LD_{95}	2.2 μg/g	In tractor oil-cyclohexanone 9:1.	1585
Musca domestica (adult)	Topical	LD_{50}	1.0 μg/g	LD_{50} parathion = 0.9 μg/g.	2231
Musca domestica (adult)	Topical	LD_{50} 24 hr.	1.3 μg/g	LD_{50} 24 hrs. parathion = 1.4 μg/g.	2247
Musca domestica (adult)	Contact Spray	LC_{50} 24 hr.	0.025 mg/cc	KD_{10} min. at LC_{50} 24 hr = 0%.	2033
Myzus cerasi	Spray	CTC_{100}*	8 oz/100 gal.	Conc. to control 100%; as metacide on 3 year old cherry trees.	102

b) Comparative toxicity methyl parathion and other insecticides:

(1) Vs. Locusta migratoria migratorioides (young virgin adults) topical application; toxicants in tractor vaporising oil + cyclohexanone (9 : 1): 1585

Insecticide		LD_{50} 96 Hrs. (μg/locust)	LD_{50} 96 hrs. (μg/g)	LD_{95} (μg/locust)	LD_{95} (μg/g)
Methyl parathion		0.94 ± 0.1	0.89	2.3 ± 0.52	2.2
Lindane		3.89 ± .21	3.69	12.9 ± 2.09	12.2
DNOC		10.4 ± .1	9.9	19.3 ± .897	18.3
Chlordane		20.4 ± 1.05	19.3	110.0 ± 30.9	104.0
Toxaphene®	(LD_{50} 5 day)	40.2 ± 2.88	38.1	123.0 ± 16.9	116.0
DDT	(LD_{50} 5 day)	140.0 ± 7.6	133.0	258.0 ± 18.6	245.0

(2) Vs. Musca domestica; topical application: 2247

Compound	LD_{50} 24 Hrs. (μg/g)
Methyl parathion	1.3
Parathion	1.4
Isopropyl parathion	4.8
Malathion	27.0
EPN®	2.0

(3) Vs. Musca domestica (adult) as contact sprays applied by turntable modification of the Peet-Grady method: 2033

Insecticide	LC_{50} 24 Hrs. (mg/cc)	KD 10 Min. At LC_{50} 24 Hrs.
Methyl parathion	0.025	0
Dieldrin	0.017	0
Parathion	0.02	0
Lindane	0.046	0
Heptachlor	0.052	0
Aldrin	0.056	0
TEPP	0.069	ca. 70%
Chlordane	0.25	0
DDT	0.35	0
Malathion	0.48	0
Toxaphene®	0.68	0
Tetrapropyl dithiopyrophosphate	0.69	0
Dilan®	0.72	ca. 30%
Isolan	1.15	100
Allethrin	1.5	100
Pyrolan	5.5	100

(4) Vs. Anopheles quadrimaculatus (4th instar larvae); laboratory tests; toxicants applied as acetone-water suspensions: 1766

Insecticide	% Mortality In 48 Hrs. At							
	0.1	0.05	0.025	0.01	0.005	.0025	0.001	0.0005
	←			(ppm)				→
Methyl parathion	100	100	100	100	100	67	—	—
Sulfotep®	100	100	100	100	100	100	74	34
Parathion	100	100	100	100	100	96	56	34
EPN®	100	100	100	100	100	96	32	—
O-(2-chloro-4-nitrophenyl)-O,O-dimethyl thiophosphate	100	100	100	96	86	62	62	44
Malathion	100	100	96	80	80	60	40	24
Ethyl O-nitrophenyl benzene thionophosphate	100	100	100	100	70	80	4	—
Diazinon	100	100	100	100	36	20	—	—
Para-oxon	100	100	100	82	50	—	—	—

(4) Vs. Anopheles quadrimaculatus (4th instar larvae); laboratory tests; toxicants applied as acetone-water suspensions: 1766

Insecticide	% Mortality In 48 Hrs. At (ppm)							
	0.1	0.05	0.025	0.01	0.005	.0025	0.001	0.0005
O-(3-chloro-4-methylumbelliferone) O,O-dimethyl thiophosphate	100	100	100	64	46	24	—	—
Chlorthion	100	100	88	76	44	—	—	—
Potasan®	100	98	56	30	5	—	—	—
O,O-diethyl O-piperonyl thiophosphate	100	94	58	26	—	—	—	—
NPD	94	—	62	30	—	—	—	—
DDT	—	—	—	100	94	49	24	—

7) Pharmacological, pharmacodynamic, physiological, etc.; insects:
   a) See the general treatment titled Organic Phosphates in this work.
   b) Converted to active anticholine esterase by intact Periplaneta americana tissues in the presence of O_2 in vitro; conversion by enzymatic action halted at 75°C. By this action methyl para-oxon $(O_2NC_6H_4O\overset{O}{\overset{/\!/}{P}}(OCH_3)_2)$ is produced. 2243
   c) Parathion resistant biotypes of Tetranychus bimaculatus, reported from certain greenhouses, are resistant also to methyl parathion with aerosol dosages which formerly yielded 100% kills for non-resistant biotypes yielding only 1% kills of the resistant types. 2867

126

MITICIDES, OR ACARICIDES

GENERAL

Many species of mites (order: Acarina; class: Arachnida) are of great importance as parasites of man and animals, and as predators and disease vectors on crop plants. These forms are not insects, and only a few of the commonly used insecticides, for example organophosphorus insecticides and dinitrophenol derivatives, have value in control of phytophagous mites.

Considerable search has been made for compounds specifically toxic to acarines, particularly because the new and potent chlorinated hydrocarbon insecticides are largely powerless against mites, and a consequence of their use has been an enormous increase in the phytophagous mite problem by destruction of natural predators.

Physiological, pharmacological, and other biological precisions, concerning miticides or acaricides are difficult because of the minute size of the arthropods in question, and a lack of detailed knowledge concerning their nature, especially their physiology.

TOXICOLOGICAL

1) This section brings together comparative data relating to various acaricidal substances to which reference will be made frequently in consideration of specific, individual compounds.

2) Toxicity of some synthetic organic and other compounds to Metatetranychus ulmi (= Paratetranychus pilosus): 900
   a) Most effective summer acaricides as shown by laboratory tests of toxicity:

Substance	Concentration % w/w	% Mortality 24 Hrs. For	
		Summer Eggs	Adult ♀♀
Bis-(p-chlorophenyl) methyl carbinol m.p. 68-69°C	0.1	97.0	100
	0.025	87.9	89.5
4-Chloroazobenzene m.p. 89°C	0.1	96.8	93.4*
	0.025	88.8	75.5
Azoxybenzene m.p. 37°C	0.1	90.5	100 *
	0.025	83.1	96.6
n-Dodecyl thiocyanate b.p. 170-2°C$^{10\text{ mm Hg}}$	0.1	86.9	96.8
	0.025	66.1	0.0
$n(C_{12}-C_{13})$ Alkyl thiocyanates (60% active ingredients)	0.1	86.0	96.6
	0.025	28.1	4.4
4-Chlorodiphenylsulfone m.p. 98°C	0.1	96.0	80.9
	0.25	73.9	65.6
Azobenzene m.p. 60°C	0.1	98.6	75.7

a) Most effective summer acaricides as shown by laboratory tests of toxicity: (continued)

Substance	Concentration % w/w	% Mortality 24 Hrs. For	
		Summer Eggs	Adult ♀♀
Azobenzene m.p. 60°C	0.05	90.5	67.7
	0.025	73.6	62.0
sec.-Dodecyl thiocyanate b.p. 155°C^{4mm}	0.1	73.9	98.2
	0.025	23.9	50.0
Diphenyl sulfone m.p. 127°C	0.1	98.1	69.3
	0.025	83.3	63.1
Hydrazobenzene m.p. 127.5°C	0.1	96.3	67.6
	0.025	93.3	43.8
	0.0125	76.0	—
N-Nitrosodiphenylamine m.p. 69°C	0.1	95.3	—
	0.05	83.9	45.6
	0.025	17.5	10.2
Bis-(p-chlorophenoxy)-methane m.p. 69-70°C	0.1	57.8	91.8
	0.025	28.9	53.1*
Tetraethyl thiuram disulfide m.p. 75°C	0.1	94.3	41.1
	0.025	71.0	—

* % Mortality in 48 hrs.

b) Toxicity of some organic compounds to winter eggs of Metatetranychus ulmi (= Paratetranychus pilosus):

Substance	Concentration (%)	% Mortality (Controls: O mortality)
Spindle-type petroleum oil	3.0 (v/v)	100
	1.5	97.3
n-Dodecyl thiocyanate	0.4	100
	0.2	98.5
Azoxybenzene	0.2	100
	0.05	87.6
Dicyclohexylamine-2,4-dinitro-6-cyclohexylphenate m.p. 190°C	0.2	99.0
	0.05	78.6
Benzaldehyde phenylhydrazone m.p. 156°C	0.2	33.7
	0.05	2.1
4-Aminobenzene m.p. 120°C	0.2	28.2
	0.05	7.8
Azobenzene	0.2	25.6
	0.05	12.6
Hydrazobenzene	0.2	9.3
	0.05	4.0
4-Hydrazobenzene m.p. 149°C	0.2	4.1
	0.05	2.0

c) Toxicity of some well known crop-protection materials for Metatetranychus ulmi:

Substance	Concentration % (w/w)		% Mortality Of	
			Summer Eggs	Adult ♀♀
Summer petroleum oil emuls. with 1% Na oleate in H_2O	1.0	(v/v)	95.3	62.0
	0.5	"	91.0	46.4
	0.25	"	76.8	30.3
	0.125	"	29.8	16.7
Rotenone (pwdrd barbasco dispersed with 1% aqueous Na oleate)	0.016	"	87.3	100
	0.008	"	86.1	100
	0.004	"	67.1	100
	0.002	"	48.1	98.6
	0.001	"	—	77.9
Summer oil + rotenone (as above)	0.5/0.004 v/v		93.0	100
	0.35/0.003 v/v		85.2	—
	0.25/0.002 v/v		74.1	100
	0.18/0.0014 v/v		56.4	—
	0.125/0.001 v/v		—	97.7
	0.063/0.0005 v/v		52.8	82.8
Lime-sulfur (sp. gr.1.3) no wetting agent.	2.0	(v/v)	56.6	—
	1.0	"	60.5	—
	0.25	"	—	98.0
	0.025	"	—	15.5
Colloidal Sulfur dispersed with 0.025% w/v Aerosol OT 100	0.5	"	11.4	—
	0.25	"	7.3	—

c) Toxicity of some well known crop-protection materials for Metatetranychus ulmi:

Substance	Concentration % (w/w)	% Mortality of	
		Summer Eggs	Adult ♀♀
Tetramethyl thiuram disulfide in H_2O medium with Aerosol 4% acetone, .05% cyclohexylamine dodecyl sulfate,.025% OT 100.	0.1	79.4	—
	0.05	—	31.3
Dicyclohexylamine-2,4-dinitro-6-cyclohexyl phenate dispersed as above.	0.1	81.3	—
	0.05	74.1	—
	0.025	—	100

d) Alkyl thiocyanates; effect on toxicity for Metatetranychus ulmi of increasing the length of the alkyl chain:

Substance	Concentration % (w/w)	% Mortality of	
		Summer Eggs	Adult ♀♀
sec.-Hexyl thiocyanate b.p. 65°C 4 mm Hg	0.1	0	0
sec.-Heptyl thiocyanate b.p. 80°C 4 mm Hg	0.1	0	4.9
sec.-Octyl thiocyanate b.p. 95°C 4 mm Hg	0.1	0	21.1
sec.-Nonyl thiocyanate b.p. 110°C 4 mm Hg	0.1	0	36.7
sec.-Decyl thiocyanate b.p. 125°C 4 mm Hg	0.1	31.0	61.4
	0.025	0	56.3
sec.-Undecyl thiocyanate b.p. 148°C 4 mm Hg	0.1	55.7	98.0
	0.025	6.2	50.8
sec.-Dodecyl thiocyanate b.p. 155°C 4 mm Hg	0.1	73.9	98.2
tert.-Butyl thiocyanate b.p. 127°C 4 mm Hg	0.025	23.9	50.0
β-Butoxy-β′-thiocyano diethyl ether 75% active ingred.	0.1	0	9.1
n-Dodecyl thiocyanate b.p. 170-2°C 10 mm	0.1	0	4.8
	0.1	86.9	96.8
	0.1	—	98.5*
	0.025	66.1	0
	0.025	—	5.7*
C_{12}-C_{13} n-Alkyl thiocyanates 60% active	0.1	86.0	96.6
	0.025	28.1	4.4
Cetyl thiocyanate b.p. 222-7°C 13 mm	0.1	88.5	22.6
	0.025	34.8	8.1

*% Mortality in 48 hrs.

e) The "diphenyl compounds" as summer acaricides; toxicity for Metatetranychus ulmi; effect of structural alterations on toxicity:

Substance	Concentration % (w/w)	% Mortality 24 Hrs. For	
		Summer Eggs	Adult ♀♀
Diphenyl m.p. 71.5°C	0.1	10.7	14.4
	0.05	—	12.4
	0.025	0	—
4,4-Diaminodiphenyl m.p. 128°C	0.1	0	0
	0.025	0	0
2,2′,4,4′-Tetranitrodiphenyl m.p. 65°C	0.1	39.8	—
	0.025	14.8	27.4
Diphenyl methane b.p. 260°C	0.1	0	47.2
	0.025	0	—
Benzophenone m.p. 45°C	0.1	0.6	57.1
Diphenyl carbinol m.p. 69°C	0.1	6.9	38.9
	0.025	2.3	—
1,1-Diphenylethane b.p. 272°C	0.1	97.0	100
	0.025	87.9	89.5
Bis-(p-chlorophenyl) methyl carbinol m.p. 68-9°C	0.1	97.0	100
	0.025	87.9	89.5
2,2-Diphenyl-1,1,1-trichloroethane m.p. 67°C	0.1	37.3	59.0
	0.025	2.8	29.6
2,2-Bis-(p-chlorophenyl)-1,1,1-Trichloroethane (DDT, m.p. 107°C)	0.1	0	50.9
	0.025	0	38.3
Dibenzyl m.p. 57°C	0.1	0	59.1
	0.05	—	33.0
	0.025	0	26.2
Benzil m.p. 96°C	0.1	0.1	65.7
	0.025	0	23.4
Benzoin m.p. 137°C	0.1	1.3	41.5
	0.05	—	31.8
	0.025	1.1	15.8
Stilbene m.p. 124°C	0.1	6.7	54.2
	0.05	—	49.5
	0.025	0	27.4

e) The "diphenyl compounds" as summer acaricides; toxicity for Metatetranychus ulmi; effect of structural alterations on toxicity: (continued)

Substance	Concentration % (w/w)	% Mortality 24 Hrs. For	
		Summer Eggs	Adult ♀♀
Dibenzoylmethane m.p. 79°C	0.1	5.2	12.0
	0.025	2.3	—
Dibenzylketone b.p. 330°C	0.1	8.2	31.8
	0.05	4.7	—
Phenylstyrylketone m.p. 61°C	0.1	34.4	91.5
	0.05	18.1	65.0
	0.025	0	50.2
α,γ-Diphenyl glycerol m.p. 127°C	0.025	0	—
Dibenzyl ether b.p. 295°C	0.1	3.8	0
	0.025	0	—
Benzyl benzoate b.p. 320°C	0.1	5.0	84.0
	0.1	—	86.3*
	0.025	0	28.6
	0.025	—	60.4*
Diphenyl carbonate m.p. 79°C	0.1	4.4	71.2
	0.1	—	76.6*
	0.025	0	50.5
	0.025	—	49.6*
Bis-(p-chlorophenoxy)-methane m.p. 69°C (Neotran®)	0.1	57.8	87.8
	0.1	—	91.8*
	0.025	28.9	56.2
	0.025	—	53.1*
Diphenylsulfone m.p. 125°C	0.1	98.1	69.3
	0.1	—	78.0*
	0.025	83.3	63.1
	0.025	—	66.8*
4-Chlorodiphenyl sulfone m.p. 98°C	0.1	96.0	80.9
	0.1	—	81.8*
	0.025	75.9	65.6
	0.025	—	75.6*
4,4′-Dichlorodiphenyl sulfone m.p. 147°C	0.1	0	—
	0.025	0	54.1
	0.025	0	52.1*
3,3′-Diaminodiphenyl sulfone m.p. 169°C	0.1	0	10.8
	0.025	0	—
4-Chloro-4′-methyldiphenyl sulfone m.p. 80°C	0.1	30.7	50.3
2,4-Dinitro-4′-methyl diphenyl sulfone m.p. 185°C	0.1	0	30.8
2,2′-Dihydroxy-5,5′-dimethyl diphenyl sulfone m.p. 197°C	0.1	0	8.6
3,3′-Dichloro-4,4′-dihydroxy diphenyl sulfone m.p. 187°C	0.1	3.9	45.0
5,5-Dichloro-2,2′-dihydroxy diphenyl sulfone m.p. 180°C	0.1	4.4	50.8
4,4′-Dihydroxy-2,2′-dimethyl diphenyl sulfone m.p. 129°C	0.1	0	24.8
4,4′-Dihydroxy-3,3′-dimethyl diphenyl sulfone m.p. 263°C	0.1	0	7.5
Diphenyl sulfide b.p. 275°C	0.1	34.0	50.3
	0.025	2.6	—
Diphenyl disulfide m.p. 66°C	0.1	0	41.3
	0.025	0	22.7
Azobenzene m.p. 60°C	0.1	98.6	75.7
	0.1	—	72.6*
	0.05	90.5	67.7
	0.025	73.6	62.0
	0.025	—	60.9*
4-Chloroazobenzene m.p. 89°C	0.1	96.8	90.6
	0.1	—	93.4*
	0.025	88.8	37.8
	0.025	—	75.5*
4,4′-Dichloroazobenzene m.p. 182°C	0.025	8.0	35.7
4-Methylazobenzene m.p. 71.5°C	0.1	77.3	59.2
	0.1	—	62.4*
	0.025	41.8	12.2
	0.025	—	29.2
4,4′-Dimethylazobenzene m.p, 141.5°C	0.1	14.3	0
	0.025	0	—
3-3′-Dimethylazobenzene m.p. 53°C	0.1	7.5	27.3
	0.025	0	0
4-Hydroxyazobenzene m.p. 149°C	0.1	0	0
	0.025	0	—

*% mortality in 48 hrs.

e) The "diphenyl compounds" as summer acaricides; toxicity for Metatetranychus ulmi; effect of structural alterations on toxicity: (continued)

Substance	Concentration % (w/w)	% Mortality 24 Hrs. For	
		Summer Eggs	Adult ♀♀
4-Aminoazobenzene m.p. 120°C	0.1	68.8	9.5
	0.025	52.6	7.7
N-Phenyldiazopiperidine m.p. 44°C	0.1	42.6	59.8
	0.025	22.8	31.8
Benzeneazo-o-cresol m.p. 128°C	0.5	0	4.0
Diazoaminobenzene	0.1	47.8	19.2
	0.025	44.8	2.7
	0.0125	17.1	—
Hydrazobenzene m.p. 127.5	0.1	96.3	—
	0.1	—	67.6*
	0.025	93.3	43.8
	0.025	—	51.6
	0.0125	76.0	—
Azoxybenzene m.p. 37°C	0.1	90.5	—
	0.1	—	100*
	0.025	83.1	96.6*
	0.0125	77.0	—
Diphenylamine m.p. 53°C	0.1	36.5	32.5
	0.05	31.0	—
	0.025	1.9	—
N-Nitroso-diphenylamine m.p. 67°C	0.1	95.3	—
	0.05	83.9	45.6
	0.025	17.5	10.2
N-Nitrosocarbazole m.p. 81.5°C	0.1	36.4	20.9
	0.025	4.4	—
Dibenzylamine	0.1	7.2	67.8
	0.025	0.7	26.8

* % Mortality in 48 hrs.

f) Toxicity of some "organophosphorus" compounds for Metatetranychus ulmi; dip tests: 899

Compound	% Mortality At Stated Concentrations For			
	Summer eggs		Adult ♀♀	
	0.1%	0.025%	0.1%	0.025%
p-Nitrophenyl diethyl thionophosphate	99.5	67.6	95.3	95.3
p-Nitrophenyl diethyl phosphate	85.1	36.5	100	98.8
Hexaethyl tetraphosphate	14.1	12.6	99.6	97.9
p-Chlorophenyl diethyl phosphate	3.4	—	—	—
p-Nitrophenyl diisopropyl phosphate	80.0	49.4	98.2	98.6
Tetraethyl dithionopyrophosphate	33.0	12.0	90.8	—
Phenyl diethyl phosphate	5.5	0	40.0	—
Diethyl 1-carbethoxyprop-1-en-2-yl phosphate	4.8	0	100	93.9
Phenyl diethyl thionophosphate	0	0	78.9	—
Tetraethyl pyrophosphate	13.2	12.7	97.9	92.2
Triphenyl phosphine	10.0	3.4	41.7	—

g) Toxicity of some "organophosphorus" compounds for overwintering eggs of Metatetranychus ulmi; dip tests; maintenance at saturation, water in air: 899

Compound	% Mortality At Stated Concentration	
	0.2%	0.05%
Triethyl phosphate b.p. 216°C	19.9	10.9
Triphenyl phosphate m.p. 49.5°C	7.6	26.8
Tri-o-tolyl phosphate b.p. 405°C	13.3	0
Triphenyl phosphine m.p. 79°C	3.0	0
Hexaethyl tetraphosphate (not distillable)	0	7.0
p-Nitrophenyl diethyl thionphosphate (75% pure)	39.1	9.6
Diethyl acetyl phosphate b.p. 110°C 6 mm Hg	0	12.3
p-Nitrophenyl diethyl phosphate b.p. 174°C 1 mm Hg	47.9	13.3
p-Nitrophenyl diisopropyl phosphate (not distillable)	20.7	13.7
Diphenyl ethyl thionphosphate b.p. 184°C 1 mm Hg	25.0	13.4
p-Nitrophenyl dichlorothion phosphonite m.p. 104°C	20.0	6.6
Diphenyl chlorothionphosphonate m.p. 64°C	9.2	8.9
Tri-(p-nitrophenyl) thionphosphate m.p. 165°C	12.9	0
Tri-(p-chlorophenyl) thionphosphate b.p. 255°C 5 mm Hg	3.6	24.6

g) Toxicity of some "organophosphorus" compounds for overwintering eggs of Metatetranychus ulmi; dip tests; maintenance at saturation, water in air: (continued) 899

Compound	% Mortality At Stated Concentration	
	0.2%	0.05%
Tetraethyl pyrophosphate b.p. 145°C 1 mm Hg.	5.4	0
Diethyl 1-carbethoxyprop-1-en-2-yl phosphate b.p. 140°C 3 mm Hg	15.9	4.6
Phenyl diethyl phosphate b.p. 136°C 1 mm Hg	11.6	10.9
p-Chlorophenyl diethyl phosphate b.p. 142°C 2 mm Hg	11.4	5.7
Phenyl diethyl thionphosphate b.p. 140°C 7 mm Hg	13.3	20.0
Triphenyl thionphosphate m.p. 48°C	22.5	0
Tetraethyl dithionpyrophosphate b.p. 130°C 2 mm Hg	5.3	0
Tetraethyl monothionpyrophosphate b.p. 133°C 2 mm Hg	0	0
Pyrophosphoric tetrakis dimethylamide b.p. 146°C 3 mm Hg	1.4	1.0
Control Hatch	81.2% hatch.	

h) Toxicity of some organic sulfur compounds to Metatetranychus ulmi: 900

Compound	Concentration % (w/w)	% Mortality 24 Hrs. For	
		Summer Eggs	Adult ♀♀
Dimethylthiuram disulfide m.p. 105°C	0.1	24.4	—
	0.05	—	56.2
Tetramethylthiuram disulfide m.p. 155°C	0.1	79.4	—
	0.05	99.5	31.3
	0.025	—	40.8
	0.0125	95.2	—
Tetraethylthiuram disulfide m.p. 75°C	0.1	94.3	—
	0.05	92.2	41.1
	0.025	—	63.5
	0.0125	71.0	—
Tetramethylthiuram monosulfide m.p. 107-8°C	0.1	80.2	—
	0.05	72.3	38.7
	0.025	—	38.7
	0.025	2.8	—
N-Diphenyl N-dimethylthiuram disulfide m.p. 199°C	0.1	6.5	—
	0.05	—	4.0
N-Diphenyl N-diethylthiuram disulfide m.p. 178°c	0.1	15.5	—
	0.05	—	16.0
Dicyclopentamethylene thiuram monosulfide m.p. 121°C	0.1	79.7	—
	0.05	21.7	21.8
	0.025	—	—
	0.0125	2.5	—
Dicyclopentamethylene thiuram disulfide m.p. 128°C	0.1	90.5	—
	0.05	42.2	42.0
	0.025	—	—
	0.0125	9.2	—
Dicyclopentamethylene thiuram hexasulfide m.p. 134-5°C	0.1	72.4	—
	0.05	15.1	77.6
	0.0125	8.8	—
Benzylamine benzyl dithiocarbamate m.p. 122°C	0.1	10.0	—
	0.025	—	24.0
Diethylamine diethyl dithiocarbamate m.p. 82°C	0.1	21.8	—
	0.025	—	0.5
n-Butyl sulfide b.p. 182°C	0.1	0	—
	0.025	—	7.1
n-Butyl disulfide b.p. 225°C	0.1	0	—
	0.025	—	0
n-Butyl mercaptan b.p. 95°C	0.1	1.7	—
	0.025	—	14.0
Thiophenol b.p. 169°C	0.1	6.8	—
	0.025	—	6.0

3) Comparison of LD_{50} and LD_{100} values of several acaricides for Tetranychus bimaculatus adult ♀♀ ; topical application in acetone solution: 1121

Substance	LD_{50}		LD_{100}	
	(??) μg/mite	mg/k	(??) μg/mite	mg/k
Etoxinol	3	150	7.8	390
Chlorobenzilate	2	100	3	150
DMC	4.2	210	8	400
Pyrazothion	2.2	120	1.2	60 (sic)

3) Comparison of LD_{50} and LD_{100} values of several acaricides for Tetranychus bimaculatus adult ♀♀ ; topical application in acetone solution: 1121

Substance	LD_{50} (??) µg/mite	LD_{50} mg/k	LD_{100} (??) µg/mite	LD_{100} mg/k
Pyrazoxon	.76	3.8	.1	5 (sic)
Diazinon	4.4	240	.2	100 (sic)
Parathion	1.8	90	4	200
Systox®	.4	20	.76	38

4) Half-life values (in days) for some acaricides in citrus peel: 1302

Substance	Half-Life (Days)	Substance	Half-Life (Days)
Aramite	7-8	EPN®	ca 80
Ovotran®	10	Parathion	60-80
DDT	30-40	Sulphenone	9-12
Dieldrin	8-10	Chlorobenzilate	60-80

5) Toxicity of some acaricidal substances for Tetranychus bimaculatus on bean plant leaves, treated in a settling tower by the method of Ebeling and Pence: 905

E = Emulsifiable concentrate; W = Wettable powder.

Compound	LC_{50} (g/100 cc) 2 Days After Treatment			
	Adults	Larvae	Eggs	Adults On Leaf Surface Opposite Treated Surface
Aramite E	.0038	.0072	.174	.041
Aramite W	.0041	.0082	.288	.055
Chlorobenzilate E	.012	.014	.078	.12
Chlorobenzilate W	.019	.019	.126	.22
DMC E	.044	.042	.082	.21
Compound 876* E	.03	.033	.079	.48
Compound 876* W	.028	.024	.15	.88
Neotran® W	.62	.215	.30	5.0 +
Ovotran® E	.45	.019	.076	5.0 +
Ovotran® W	4.25	.028	.109	5.0 +
R-242**E	.21	.23	.35	4.6
R-242**W	.27	.26	.89	5.0 +
Compound 923***E	.78	.21	.39	5.0 +
Compound 923***W	1.55	.48	.67	5.0 +
Karathane****E	.036	.013	.24	1.43
Karathane****W	.066	.027	.53	3.6
DN-111 W	.082	.031	.28	1.44
DN-289 E	.0083	.0072	.038	.24
Parathion E	.0056	.013	.19	.021
Parathion W	.0045	.010	.37	.027
Malathion E	.0025	.0073	.32	.084
Malathion W	.0042	.0115	.84	.125
EPN E	.0025	.0047	.23	.042
EPN W	.0048	.0077	.46	.076
Diazinon W	.012	.028	.18	.115
Demeton E	.0022	.0028	.097	.003

* = Bis-(p-chlorophenyl)ethinyl carbinol.
** = p-Chlorophenyl sulfone.
*** = 2,4-Dichlorophenyl benzene sulfonate.
**** = Dinitrocapryl phenyl crotonate.

6) LC_{50} and LC_{90} values of various acaricides vs. Tetranychus bimaculatus red and green forms; dips and sprays on red kidney bean leaves: 565

Compound	Method	Time Of Mortality Count	LC_{50} (ppm)		LC_{90} (ppm)	
			Red Form	Green Form	Red Form	Green Form
TEPP	dip	24 hr.	3.8	2.5	13.0	17.0
EPN®	dip	24 hr.	5.5*	3.9*	20	12
Malathion	dip	48 hr.	36 **	48 **	96	120
DMC	dip	24 hr.	9.6	6.8	26.5	20
DMC	dip	48 hr.	8	6	28.5	19
DMC	dip	72 hr.	7.9	4	17.5	12
DMC	spray	48 hr.	31	26	78	60
Aramite	dip	48 hr.	2.9	2.9	18	19.5
Aramite	spray	48 hr.	22	14	93	72

a) No significant difference in susceptibility between color forms save at: * (= significance at 5% level) and at ** (= significance at 2% level).

7) Acaricides vs. Metatetranychus ulmi on Northern Spy apple trees under New York conditions in 1952: 1990

Compound	Dosage lbs/100 gal.	% Reduction Of Mites On Days After July 4 Sprays		
		3 days	10 days	17 days
O,O-Diethyl 0-2 (ethyl mercaptoethyl thiophosphate (42% liquid)	2 oz	98.5	100	100
" " " " "	4 oz	99.1	100	99.9
Ethoxymethyl-di-(p-chlorophenyl)carbinol (25% emuls.)	1 pint	98.5	87.5	83.7
2-Hydroxy-2,2-bis-(4-chlorophenyl)ethyl acetate(Chlorobenzilate) 25% emuls.	1 pint	99.0	95.8	95.6
O,O-Diethyl O-(2-isopropyl-4-methylpyrimidyl)(6)thiophosphate 25% emuls.	1 tp	95.6	94.6	89.5
O,O-Diethyl O-5(3-methyl pyrazolyl)thiophosphate (25% emuls.)	1 pint	96.2	99.8	99.8
Diethyl-5-(3-methyl pyrazolyl) phosphate (25% emuls.)	1 pint	95.3	98.8	98.6
Malathion (25% wett. pwdr.)	2	97.2	99.6	98.6
Malathion (50% emuls.)	1 pint	96.5	98.7	96.9
Parathion (15% wett. pwdr.)	1	98.7	99.8	99.5
Tetra-n-propyl dithionopyrophosphate (NPD)(25% wett. pwdr.)	2	99.3	98.5	97.3
Phenyl mercuric acetate (10% liquid)	0.5 pint	91.7	71.5	—
2-Heptadecyl glyoxalidine acetate (34% liquid + 3 lb lime)	2 pints	96.6	67.9	—
Sulphenone® (50% wett. pwdr.)	3	94.4	94.9	94.6
Aramite (15% wett. pwdr.)	1.5	98.1	98.5	97.1
CONTROL (Average no. of hatched mites/leaf)		239	104	59

a) Also available from this source, data on efficiency vs. winter eggs and new-hatched larvae.

8) Evaluation by field tests of acaracides in control of Aceria sheldoni. Sprays; by sampling 10 new growth terminals from each of 8 trees, 5 buds of each terminal dissected and count of mites determined. Degree of control in preliminary trials: 1699

a) Good control:

Dicyclohexylamine of 4,6-Dinitro-o-sec.-butyl phenol (DN-211)(wett. pwdr.)
Di-2-ethyl hexyl phthalate (emuls.)
DDT (in kerosene) (emuls.)
Chlordane (emuls.; wett. pwdr.)
Aramite® (emuls.; wett. pwdr.)

b) Fair control

EPN (emuls.; wett.pwdr.)
Xanthone (wett. pwdr.)
Methylated naphthalenes (AR-70)(emuls.)
Dioctyl fumarate (emuls.)
Dioctyl sebacate (emuls.)
Lethane 60
OMPA
Parathion

c) Poor or no control

2,2-Bis-(p-butoxyphenyl) propane (emuls.)
1,1-Bis-(p-chlorophenyl) ethanol (DMC)(emuls.; wett. pwdr.)
Lorol-2-thiazolinyl sulfide (emuls.)
Bis-(p-chlorophenoxy)-methane (emuls.; wett. pwdr.)
p-Chlorophenyl-p-chlorobenzene sulfonate (emuls.; wett. pwdr.)
Dicyclohexylamine salt of DNOCHP (wett. pwdr.)
4,6-Dinitro-2-capryl phenyl crotonate (wett. pwdr.)
2,4-Dichlorophenyl benzene sulfonate (emuls.; wett. pwdr.)
p-Chlorophenyl phenyl sulfone (emuls.; wett. pwdr.)
1,1-Bis-(X-chlorophenyl)-ethane (emuls.)
Hydroxy pentamethyl flavan (wett. pwdr.)
Toxaphene (wett. pwdr.)
BHC (wett. pwdr.)
Aldrin (emuls.; wett. pwdr.)
Dieldrin (emuls.; wett. pwdr.)
1,1-Dichloro-2,2-bis-(p-chlorophenyl)-ethane (wett. pwdr.)
Diphenyl oxide (emuls.)
Diphenylamine (emuls.)
Piperonyl cyclonene (emuls.)
Benzyl benzoate (emuls.)

c) Poor or no control (continued)

Thialdine (emuls.)
N-Butyl-butyrol thialdine (emuls.)
Phenothiazine (emuls.; wett. pwdr.)
Phenothioxin (emuls.)
Polyethylene polysulfides (wett. pwdr.)
Methyl N-amyl ketone (emuls.)
Tetraethyl pyrophosphate (emuls.)

9) Comparative effectiveness of some acaricides vs. Septanychus texazona and Tetranychus bimaculatus, at the 95% mortality level: 2277

Acaricides formulated in miscible oil concentrates; applied at rate of 21.5 gals. per acre.

	Acaricide	Lbs/Acre Required To Give			
		50% Kill	95% Kill	50% Kill	95% Kill
		S. texazona		T. bimaculatus	
		1 day after application to cotton plants with adult mites			
(I)	Aramite®	0.087	0.474	0.166	5.64
(II)	p-Chlorophenyl phenyl sulfone (R-242)	.478	3.659	1.712	90.49
(III)	Parathion	.008	.066	.057	4.11
(IV)	Merthon*	.070	2.353	.155	52.24
		3 days after application			
(I)		.112	3.044	.150	11.13
(II)		.636	20.99	1.95	168.4
(III)		0.31	3,053.0 (?)(sic)	.134	627.0
(IV)		.202	677.8	.175	1,429.0
		5 days after application			
(I)		.074	.660	.076	6.05
(II)		.435	7.38	1.108	83.03
(III)		.011	.985	.027	.70
(IV)		.031	139.9	.103	6.99

* = Mercurated pentaethyl triphosphate and related phosphates:

a) Comparative effectiveness (> = Significantly More Effective Than)

Days after application	Order Of Effectiveness Vs.
1	S. texazona: Parathion > Aramite > Merthon > R-242.
1	T.bimaculatus: Parathion > Aramite > Merthon > R-242.
3	S. texazona: Aramite > R-242 > Parathion > Merthon.
3	T. bimaculatus: Aramite > Parathion = R-242 > Merthon.
5	S. texazona: Parathion = Aramite > R-242 > Merthon.
5	T. bimaculatus: Parathion > Aramite = Merthon > R-242.

10) Acaricidal properties; compounds related to DDT and other substances; acaricidal and insecticidal activity compared: 2230

Compound	LC$_{50}$ 24 Hrs (% Concentration) For	
	Heliothrips haemorrhoidalis (Insect)	Paratetranychus citri (Acarine)
DDT	0.001	non-toxic at 10.0
Toxaphene®	.0025	non-toxic at 1.0
γ-BHC	.0001	1.0
Chlordane	.0035	1.0
Tetraethyl pyrophosphate	.0003	.0005
Parathion (95% tech.)	.0001	.0001

Relative toxicity of some acaricides vs. Paratetranychus citri and Tetranychus bimaculatus:

Compound	LC$_{50}$ 24 Hrs (% Concentration) For	
	P. citri	T. bimaculatus
1,1-Bis-(p-chlorophenyl) ethanol	0.1	0.035
Bis-(p-chlorophenoxy)-methane	.025	> 1.0
Bis-(p-chlorophenyl)-methane	.25	.25
2-(p-Chlorophenyl)-1,1,1-trichloroethanol	.2	.4
p-Chlorobenzyl-p-chlorophenyl ether	.13	—
Di-p-chlorophenyl ether	1.0 (LC$_{57}$)	—
p-Chlorophenyl-p-chlorobenzoate	1	—
Bis-(p-methyl phenoxy)-methane	.09	—
Bis-(p-bromophenoxy)-methane	.1	—
p-Chlorobenzyl-p-bromophenyl ether	.9	—

(1) Order of acaricidal effectiveness in p, p′ substituents of Bis-phenoxymethane:

$$Cl < Br < CH_3 < NO_2 < CH_3O$$

(2) This same source evaluates ca. 100 compounds vs. P. citri and H. haemorrhoidalis.

11) Residual toxicity of certain acaricides for Tetranychus bimaculatus; greenhouse tests on Phaseolus coccineus plants: 117

Substance	Lbs/100 Gals. Formulation	Lbs/100 Gals. Active	% Mortality On Days Between Spray And Infestation: 1 day	3 days	7 days	10 days	14 days
Ethyl p-nitrophenyl thionobenzene phosphonate (EPN) 31.5% pwdr.	0.25	0.079	100	100	99.7	100	80
1,1-Bis-(p-chlorophenyl)-ethanol (DMC) 50% pwdr.	0.5	.25	99.9	100	86	99.5	89.4
p-Chlorophenyl-p-chlorobenzene sulfonate (C-854) 50% pwdr.	2.0	1.0	90.3	75.6	82.8	91.4	80.3
Dinitro-o-cyclohexylphenol (DNOCHP) 40% pwdr.	0.78	.31	100	94.8	80	99.6	61
Bis-(p-chlorophenoxy)-methane (Neotran®) 40% pwdr.	2.5	1.0	86.9	85.4	93.3	55	15.7
β-Chloroethyl-β-(p-tert-butyl phenoxy)-α-methyl ethyl sulfite (88R) 15% pwdr.	1.25	.188	98.3	97.4	72.0	47.0	17.3
Parathion (15% pwdr.)	2.0	.3	99.8	94.4	54.3	51.6	19.5
Dinitro-capryl phenyl crotonate (Arathane) 25% pwdr.	2.0	.5	90.2	84.8	24.0	34.3	52.1
Lauryl-2-thiazolinyl sulfide (IN-4200) 75% emuls.sol.	1:800	.75	85.4	91.0	26.9	18.7	8.4
Dinitro-o-cyclohexyl phenol (DNOCHP) 40% pwdr.	.39	.16	72.6	70.2	32.0	23.4	10.7
" " " " , NH_4 salt	.78	.31	92.6	70.1	33.0	37.9	19.8
" " " " , Monoethanolamine salt	.78	.31	89.6	69.8	40.0	26.0	14.5
2,4-Dichlorophenyl benzene sulfonate (50% emuls. sol.)	1:400	1.0	46.8	41.6	12.1	32.6	27.6
DNOCHP, NH_4 salt	.39	.16	26.7	25.2	16.3	13.9	14.5
" , Monoethanolamine salt	.39	.16	21.2	11.6	10.3	6.1	8.3

a) DMC, EPN, p-Chlorophenyl benzene sulfonate, (most efficient):	Residual toxicity lasted 14 days.
b) DNOCHP (5 oz/100 gal.)	" " " 10 " .
c) 88 R, Neotran®	" " " ca.7 days.
d) Parathion	" " " ca.6 days.
e) Arathane	" " " ca.5 days.
f) Lauryl-2-thiazolinyl sulfide	" " " ca. 3-5 days.
g) Salts of DNOCHP (5 oz/100 gal.)	" " " ca. 3 days.
h) 2,4-Dichlorophenyl benzene sulfonate	Little if any residual action.

12) Qualitative evaluation of acaricides for control of orchard mites; preventive schedules to control acarines on apples (variety = Delicious) under Southern California conditions: 191

a) To control Tetranychus bimaculatus (in absence of reinfestation from orchard cover):

1,1-Bis-(p-chlorophenyl)-methylcarbinol = 2-(p-tert.-Butyl phenoxy) isopropyl-2-chloroethyl sulfite = OMPA > p-Chlorophenyl-p-chlorobenzene sulfonate > p-chlorophenyl phenyl sulfone > Ethyl-p-nitrophenyl thionobenzene phosphonate (EPN) = Parathion > Dicyclohexylamine dinitro-o-cyclohexylphenate > 2,4-Dichlorophenyl-benzene sulfonate.

b) To control Paratetranychus pilosus:

2-(p-tert.-Butylphenoxy)-isopropyl 2-chloroethyl sulfite = 1,1-Bis-(p-chlorophenyl)-methyl carbinol = EPN = Octamethyl pyrophosphoramide (OMPA) = 2,4-Dichloro-phenyl benzene sulfonate = p-Chlorophenyl phenyl sulfone > p-Chlorophenyl-p-chlorobenzene sulfonate = Parathion > Dicyclo hexylamine dinitro-o-cyclohexyl phenate.

c) To control Bryobia praetiosa:

Dicyclohexylamine dinitro-o-cyclohexyl phenate = Parathion - 1,1-Bis-(p-chlorophenyl)-methylcarbinol > p-Chlorophenyl-p-chlorobenzene sulfonate = 2,4-Dichlorophenyl benzene sulfonate > 2-(p-tert.-Butylphenoxy)-isopropyl-2-chloroethyl sulfite = p-Chlorophenyl phenyl sulfone > EPN.

d) In preventive schedules for T. bimaculatus on Bartlett pear trees subject to reinfestation from orchard cover:

p-Chlorophenyl-p-chlorobenzene sulfonate = 2-(p-tert.-Butylphenoxy)-isopropyl 2-chloroethyl sulfite > p-Chlorophenyl phenyl sulfone > EPN > 2,4-Di-chlorophenyl benzene sulfonate > Parathion.

e) Compounds found to have acaricidal properties worthy of further test:
(1) O,O-Dimethyl-S-(2-oxo-ureido-ethyl) dithiophosphate.
(2) S-Carbamyl methyl-O,O-dimethyl dithiophosphate.
(3) S-(1,2-Dicarbethoxyethyl)-O,O-dimethyl dithiophosphate.
(4) S-(1,2-Dicarbethoxyethyl)-O,O-diethyl dithiophosphate.

f) Compounds of relatively low acaricidal effectiveness:
(1) 1,1-Bis-(x-chlorophenyl)-ethane.
(2) O-(2-Chloro-4-nitrophenyl)-O,O-dimethyl dithiophosphate.

- g) Phytotoxicity:
    - (1) Russetting (Delicious apples)—Bis-(p-chlorophenoxy)-methane.
    - (2) Skin blackening in stem pit —p-Chlorophenyl-p-chlorobenzene sulfonate.
    - (3) Fruit spotting (Bartlett pears)--Alkyl-2-thiazolinyl sulfide.
    - (4) Slight russetting (Bartlett pears)—2-(p-tert.-Butyl phenoxy)-isopropyl 2-chloroethyl-sulfite.
- h) Parathion (15 and 25% active ingredient as wettable powder) on apples gave 85% control of Tetranychus bimaculatus and Paratetranychus pilosus; 92% preventive control of Bryobia praetiosa (63% corrective control). Several sprays at 4 weeks intervals necessary for control of T. bimaculatus and P.pilosus as a mixed infestation.

13) Acaricides for control of Paratetranychus pratensis (most injurious of wheat pests in New Mexico): 1442

- a) Systox and Parathion gave best control; Chlorobenzilate® yielded erratic results; Ovotran®, malathion, EPN, Schradan, Metacide®, methyl parathion, Aramite®, DMC, R-242, Compound 823, dieldrin gave less than 75% mortalities.

14) Acaricides; order of effectiveness vs. Petrobia latens on dryland wheat in lbs. per acre. Based on counts made 5 days and 2 weeks after treatment: 1482

Demeton 0.5 > parathion 0.5 > parathion 0.25 = demeton 0.25 > Metacide® 0.25-0.5 = Schradan 0.5 > NPD 0.5-1.0 > chlorobenzilate® 0.5 = Aramite® 0.33-0.66 = Ovotran® 0.5-1.0 = compound 923 1.0-2.0 > TEPP 0.25-0.5 = EPN 0.5 = malathion 0.75-1.5 = R-242 1.0-2.0 = Toxaphene® 3.0 Compound 876 0.5 = endrin 0.15-0.3 = DMC 0.25-0.5 > BHC 0.5-1.0.

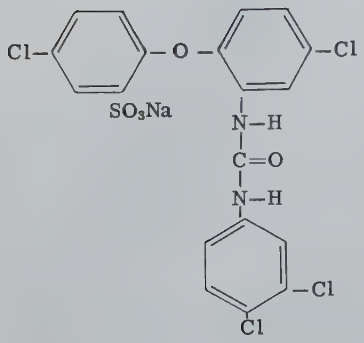
15) Acaricides in control of orchard mites; apple orchards in Pacific Northwest: 727

- a) Parathion at 0.75 lb (15% concentrate)/100 gal. controlled Tetranychus bimaculatus, Bryobia praetiosa, Metatetranychus ulmi.
    - (1) Insufficient to control Tetranychus pacificus and Eotetranychus carpini borealis.
- b) Malathion at 0.5 pint (50% concentrate) or 1 lb wett. pwdr. (25%)/100 gal. controlled above mites with exception of E. carpini borealis.
- c) EPN at 0.5 lb (27% wett. pwdr.)/100 gal. controlled excellently the foregoing mites with exception of E. carpini borealis.
- d) Metacide® 33% concentrate at 1 pint/100 gal. controlled T. bimaculatus, B. praetiosa, M. ulmi, but not T.pacificus or E. carpini borealis.
- e) Toxaphene is of value vs. Bryobia praetiosa but, by comparison, relatively ineffective against others here mentioned.
- f) DMC (25% concentrate) gave longer residual effectiveness than any non-systemic insecticide; 1.5 pints/100 gal., in June, usually controlled all species for the season.
- g) Aramite showed a selective effect:

    1 lb. 15% wett. pwdr./100 gal. controlled T. pacificus.
    2 lb. 15% wett. pwdr./100 gal. controlled B. praetiosa, M. ulmi.
    1/2 pint emulsifiable concentrate/100 gal. controlled T. bimaculatus, M. ulmi, but gave only fair control of B. praetiosa, T. pacificus, E. carpini borealis.
- h) p-Chlorophenyl-p-chlorobenzene sulfonate: Poor control of T. pacificus at 1.5 lb 50% wett. pwdr/100 gal. At 1 lb. 50% wett. pwdr./100 gal. gave good control of other species.
- i) p-Chlorophenyl phenyl sulfone (40-50%) at 2-3 lb/100 gal. yielded results closely like (h) except for less effective control of E. carpini borealis.
- j) Systox showed longer residual effectiveness than Schradan.

127

MITIN (N-(3, 4-Dichlorophenyl)-N′-2-(2-sulfo-4-chlorophenoxy)-5-chlorophenyl urea, Sodium salt)



GENERAL

A mothproofing agent for the treatment of woolen fabrics, etc. Treated wool cannot be distinguished from untreated wool by appearance, handling characteristics, color, odor, softness or other qualities. Draws completely from the dyebath into the wool, having the characteristics of a colorless wool dye-stuff. Compatible with most dye-stuffs used in the acid-dyeing of wool. Maximum fastness is achieved when applied in an acid bath at (or near) boiling for 30 to 60 minutes. At lower temperatures a longer time for fixation must be allowed. Dosages may be expressed in percent of weight of wool, for instance 2 lbs Mitin in a bath in which 100 lbs. of wool have been treated have a dosage value of 2% of wool weight after drying, because of complete fixation to the wool. 982

PHYSICAL, CHEMICAL

A white, odorless powder; soluble in water to 0.05% at room temperature; at 160°F 0.4 g dissolve in 100 cc of water, at 180°F 1.5 g dissolve in 100 cc of water, at 212°F 5.5 g dissolve in 100 cc of water.

a) Formulation: As Mitin FF concentrate, with 42.5% active ingredient.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) No data available to this compilation. Presumably non-toxic as a fabric-protecting agent.

2) Toxicity for insects:
   a) Vs. *Tineola bisselliella* at 1.0%: 100% kills of 7 day old larvae in 7 days, of 14 day old larvae in 14 days, of 25 day old larvae in 21 days; at 1.5%: 100% kills of 7 day and 14 day old larvae in 7 days, 25 day old larvae in 21 days; at 2.0%: 100% kills of 7 and 14 day old larvae in 7 days, 25 day old larvae in 14 days.
   b) Weight loss tests; *Tineola bisselliella* on wool fiber:

Treatment	Average Wgt. Loss (%)	% Kill In			
		7 days	14 days		
2% Mitin	2.2	90	100		
Untreated	86.9	0	0		
On flannel "baited" with brewers' yeast:		3 days	7 days	10 days	14 days
2% Mitin	3.1	66	93	99	100
Untreated	103	4	5	5	5

   c) Vs. *Attagenus piceus*; weight loss tests of carpets, yarns and coating treated with 2% Mitin baths:

Material	Conc. Mitin % (By Analysis)	Av. Wgt. Loss (mg)	% Mortality In	
			7 days	14 days
Wool cloth	1.3	1.7	85	100
Flannel	2.0	2.2	90	100
High pile fabrics	1.9	5.1	85	100
Low pile fabrics	2.0	2.5	86	100
Felt	1.8	2.2	40	95
Felt	—	2.6	83	98

(1) Dosage mortality data on wool fiber:

Mitin Conc. (%)	Age Larvae (weeks)	% Mortality At				Average Excrement Wgt. (mg)
		7 days	14 days	21 days	28 days	
0.625	4	19	84	98	100	0.7
"	8	5	5	10	70	3.9
"	12	0	0	0	0	9.4
"	16					10.7
1.25	4	63	100	—	—	0.6
"	8	15	30	35	75	1.6
"	12	0	0	0	0	5.5
"	16					5.1
2.5	4	79	100	—	—	.7
"	8	5	25	40	95	1.6
"	12	0	0	0	0	3.8
"	16					3.2
Untreated	4	5	5	8	8	3.6
"	8	0	0	0	0	19.0
"	12					25.3
"	16					17.8

(2) Vs. Anthrenus vorax:

Mitin Conc. (%)	Age Larva (weeks)	Mg Excrement In 14 Days
0.625	4	2.1
"	6	6.4
"	8	4.3
1.25	4	1.0
"	6	4.2
"	8	2.0
2.5	4	1.4
"	6	3.1
"	8	1.6
Untreated	4	14.6
"	6	45.8
"	8	27.4

(3) Vs. Attagenus piceus:

Material	% Mitin By Analysis	Average Excrement (mg) In	
		14 days	28 days
Carpet	1.6	4.0	5.1
Knit goods	2.0	1.8	1.9
Cashmere	1.8	3.3	4.4
Yarn	1.7	2.7	3.2
Fabric	2.2	3.4	3.8
Coating	1.9	3.8	4.6
Serge	2.5	1.9	2.6
Socks	1.4	1.9	2.1
Felt	1.9	2.5	2.8
Yarn	2.2	1.6	1.7

(4) Fastness to standard flannel; 2% applications of Mitin:

Treatment	Attagenus	Tineola
	Average Excrement 4 Wks. (mg)	(% Kill in 2 Wks)
Dry cleaned 30 times	3.2	100
Original	4.4	100
Control	42.3	0
Washed (machine) 25 times	5.1	100
" " 5 times	5.2	100
" " 25 times	6.4	95
Original	4.6	100
Control	40.0	0

(5) Effectiveness after 5 years storage of treated materials:

Material	Attagenus	Tineola
	Average Excrement 2 Wks. (mg)	% Kill (2 Wks.)
Flannel	4.2	95
Camels' hair (unbleached)	3.7	100
" " (bleached)	4.5	100

128

MOSQUITO LARVAE; BODY LICE: TESTS OF INSECTICIDES AGAINST

1) Evaluation of the effectiveness of some present day insecticides against 4th instar larvae of Anopheles quadrimaculatus and young adult Pediculus humanus corporis in laboratory tests: 2020

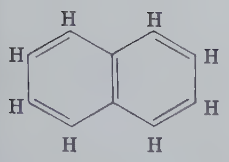
Insecticide	A. quadrimaculatus Larvicide			Body Lice	
	Least p.p.m. 100% Effective	Next lower Dosage: P.p.m.	% Kill	100% Knockdown Time (Hours)	Days 100% Effective
Aldrin	0.025	0.01	98	1	31+
Allethrin	.2	.1	76	1	31+
Anabasine	—	—	—	—	—
BHC	.2	.1	92	—	30-31
Chlordane	.01	.005	52	3	31+
TDE	.005	.0025	95	6-24	0-1
DDT	.01	.005	66	6	31+
DFDT	.025	.01	85	6	31+
Dieldrin	.005	.0025	90	3	31+
Dilan®	.1	.05	94	24	7-8
DNBP	10.0	1.0	0	0.25	30-31
DNCHP	10.0	1.0	50	3	31+
DNOC	10.0	1.0	10	1	31+
Endrin	—	.01	96	1	31+
EPN®	.005	.0025	96	24	31+
Heptachlor	.025	.01	79	—	31+
Isodrin	1.0	.1	78	3	31+
Isopestox®	—	—	—	—	—
Lethane 60®	—	10.0	20	0.5	16
Lethane 384®	—	10.0	20	1	31+
Lindane	.05	.025	62	0.5	31+
Malathion	—	.025	96	1	31+
Methoxychlor	.1	.05	45	24+	0
Methyl parathion	.005	.0025	67	0.25	31+
Nicotine	—	10.0	15	—	—
Para-oxon	.025	.01	82	—	31+
Parathion	.0025	.001	80	0.25	31+
PDB	—	10.0	70	24+	0
Pentachlorophenol	10.0	1.0	45	1	30-31
Phenothiazine	1.0	.1	5	24+	0
Potasan®	0.1	0.01	18	0.5	31+
Pyrolan	—	10.0	98	1	31+
Pyrethrins	.1	.05	78	.25	30-31
Rotenone	10.0	1.0	60	24+	0
Ryania	—	—	—	—	—
Sabadilla	—	—	—	3	31+
Schradan	—	10.0	42	6	31+
Sulfotepp®	.0025	.001	74	.5	31+
Systox®	.1	.01	6	.25	31+
TEPP	10.0	1.0	42	1	3-7
Thanite®	10.0	1.0	5	3	31+
Toxaphene®	.01	.005	80	—	31+

a) Tests on mosquito larvae were performed by exposing insects for 48 hours in serial dilutions of the tested compounds prepared by mixing acetone solutions of the toxicants in water.

b) Tests on body lice were performed by dipping woolen patches in 1% solutions of the test compounds, allowing the patches to dry, and then exposing young adult lice to the patches for 24 hours in beakers. Patches on which all lice were dead or in the "knocked down" state were retained and tested again at frequent intervals until one or more insects remained unaffected after a 24 hour exposure.

129

NAPHTHALENE (Naphthalin; Naphthene; Tar camphor; "Moth Balls, Flakes.")



Molecular weight 128.16

GENERAL [Refs.: 353,2120,3003,3004,129,2867,2621,1218,3033,406,2616,3054,1,3117,3291,1925,539,314, 2260,1976,1801]

A low toxicity fumigant of very limited usefulness, employed mainly as a household insecticide to protect furs and woolens against moths. Employed in a limited way as a soil fumigant vs. larvae of Popillia japonica. A high minimum concentration, often to be achieved only by artificial means (heat, vaporizing devices, aerosols), is required for effectiveness, but even at saturation in air toxicity for insects is low. Thermally vaporized, it may be used to control certain greenhouse mites, for instance red spider, on some plants which tolerate it under high temperature and high humidity, conditions. Synergizes with nicotine vs. Trialeurodes vaporariorum; 0.56 mg/l naphthalene + 0.004-0.006 mg/l nicotine vapor gives more rapid "knockdown" than either alone. Some effectiveness vs. Musca domestica as an aerosol, if dispersal is prolonged by combination with a "smoke." Halogen derivates of naphthalene are moderately insecticidal, for example, α-chloronaphthalene is 8 times more toxic than naphthalene, and β-chloro-, bromo-, iodo- derivatives are effective against some caterpillars. Other relatives such as 3-chloroacenaphthene, 2-chlorofluorene and 9-bromophenanthrene, are effective as aerosols vs. Musca domestica. Naphthalene is the most abundant single constituent of coal tar and as an abundant constituent of industrial wastes is of importance to hydrobiologists and conservationists. Rapidly decomposed by microflora in the soil.

PHYSICAL, CHEMICAL [Refs.: 2221,2671,353,129,2120,321,539]

A solid in colorless, crystalline flakes which may be compressed or moulded into various forms such as cakes, balls, granules etc.; m.p. 80.2°C; b.p. 217.9°C; $d_{4°}^{20°}$ 1.162; $n_D^{100°}$ 1.582; v.p. 4.92×10^{-2} mmHg at 20°C; virtually insoluble in water (to 30 ppm at 20°C); slightly soluble in alcohol, 1g/13cc; soluble in benzene, toluene 1g/8.5cc, olive oil, turpentine 1g/8cc, chloroform, carbon tetrachloride 1g/2cc, carbon disulfide 1g/1.2cc; very soluble in ether, hydronaphthalenes, fixed and volatile oils; characteristic odor; flammable but safe at ordinary temperatures; flash point (open cup) 79°C, 174°F; 1 mg/l = 191 ppm, 1 ppm = 0.00524 mg/l; volatile in steam.

Vapor Pressure and maximum amounts (lbs/1000 ft^3) which can exist at various temperatures:

Temp °F	V.P. mmHg	Lbs/1000 ft^3	Temp °F	V.P. mmHg	Lbs/1000 ft^3
32	.02	.01	86	.14	.06
59	.06	.03	95	.21	.09
68	.08	.035	104	.32	.13
77	.1	.04	113	.51	.21
			122	.81	.32

a) Formulation: Pure, or impure, in crystals, flakes, molded forms; sometimes perfumed; as an anti-clothes-moth spray, 30% in CCl_4.

TOXICOLOGICAL

1) Toxicity for higher animals: 851
   a) Toxic for mammals only in comparatively large doses. 2 to 3 g reported to consitute a fatal dose for man. 1665
   More toxic, orally, in the presence of oil. Large volumes of the vapor may be toxic. Self-warning by odor 129
   and irritation. 539
   b) Toxicity for fish:

Sunfish	LC	4-5 ppm	Death in 1 hr.	2811,1309
Sunfish	LC	10 ppm	"	754,939
Perch	LC	40 ppm		1714
Minnows	Toxic Effects	17.1 ppm	Exposure 1 hr.	2751

   c) Chronic exposure:
   (1) Concentrated fumes are damaging to the eyes; irritant to the skin and mucous membranes on contact. 129
   Avoid prolonged exposure to vapors.
   d) Symptoms:
   (1) Smarting of eyes, throat irritation; if taken orally excessive vomiting and abdominal pain followed by 129
   nephritis. Prolonged breathing of vapors may produce delirium. 539

2) Phytotoxicity:

a) Very phytotoxic, with some selective effect. Accumulation in the soil is prevented by rapid microbial decomposition. 129 1424

3) Toxicity for insects:

a) Approximate time of exposure required for 100% mortality (at 48 hrs) of various insects exposed to atmospheres saturated with naphthalene; estimates from diagram: 2556

Insect	Lethal Time$_{100}$ (48 Hrs)
Muscina stabulans	ca. 1 hr
Drosophila	ca. 2 hrs
Millipedes	ca. 3 hrs
Menopon biseriatum	ca. 4 hrs
Sowbug	ca. 6 hrs
Tribolium confusum	ca. 12 hrs
Tenebrio molitor	ca. 18 hrs
Bruchus obtectus	ca. 42 hrs

b) Toxicity to Tenebrio molitor (larva) by injection in olive oil solution; estimates from a series of graphs in the cited reference: 2556

Dose (μg/pupa)	% Mortality	Time
41.6	ca 40	In 3 days
83.2	ca 50	In 6 " ; ca 90% in 10 days.
124.8	ca 50	In 2 " ; ca 100% in 8 days.
208.0	ca 50	In 1 " ; ca 100% in 5-7 days.
416.0	ca 50	Immediate; ca 100% in 2 days.

c) Exposure of eggs of Bruchus obtectus and Tenebrio molitor to atmospheres saturated with naphthalene at 25°C, 70% relative humidity; eggs 0 to 1 day old; control hatches: Bruchus = 91-96%, Tenebrio = 89-91%: 2556

Exposure Time (Hrs)	% Hatch Treated Eggs Of	
	Bruchus obtectus	Tenebrio molitor
0.5	—	85
1	87	72
1½	—	48
2	80	25
2½	—	8
3	45	1
4	14	—
5	6	—
6	0.4	—

(1) Age of eggs and toxicity of naphthalene:

Age Of Eggs (Days)	% Mortality Of Eggs After 3 Hrs Exposure of	
	Bruchus obtectus	Tenebrio molitor
0-1	55	99
1-2	70	83
2-3	71	38
3-4	81	12
4-5	90	10
5-6	68	11
6-7	22	15
7-8	—	23
8-9 (larvae)	—	0
9-10 (larvae)	—	0

d) Life-cycle stages of Tenebrio molitor and toxicity of naphthalene: 2556

Larvae (Age)	Weight (mg)	% Mortality (Exposure 16 Hrs To Naphthalene At Saturation)
2 days	0.47	100
1 month	.77	98
2 months	1.53	86
"	8.37	32
3 "	4.85	60
"	11.32	48
"	13.47	32
"	20.32	16
4 months	5.46	48

d) Life-cycle stages of Tenebrio molitor and toxicity of naphthalene:

Larvae (Age)		Weight (mg)	% Mortality (Exposure 16 Hrs To Naphthalene At Saturation)
4 months		36.0	4
Full grown		152.7 (average)	20 (24 hr exposure)
Pre-pupae			94
"	(0-2 days old)		38
Pupae	(6-8 days old)		40
"	(8-10 days old)		86.6
Adults	(0-7 days old)		100

(1) In case of eggs, toxicity is directly related to respiratory and metabolic rate; increased weight loss is associated with increased toxicity. Development of Bruchus eggs was retarded by sub-lethal exposures to naphthalene vapor. Developmental rate of Tenebrio eggs was not affected by sub-lethal exposure; subsequent growth was unaffected.

e) Synergistic action with nicotine; comparative efficiency of naphthalene alone at 0.56 mg/l and of naphthalene (.56 mg/l) combined with 0.006 mg/l nicotine vapor (a sub-lethal concentration) vs. Trialeurodes vaporariorum; 25°C, relative humidity ca. 0%: 2621

Exposure (Minutes)	% Mortality With	
	Naphthalene (0.56 mg/l)	Nicotine (0.006 mg/l) + Naphthalene (0.56 mg/l)
45	47.9	73.0
45	31.6	72.7
60	61.0	96.8
60	76.3	96.7
60	46.1	96.8
75	89.8	100
75	73.3	99.3
75	75.2	100

4) Pharmacological, pharmacodynamic, physiological, etc.; insects:

a) Considered to be a liposoluble neurotoxic agent, inducing, in insects, a slow paralysis. 2556,3278

(1) Arthropod nerve (naphthalene poisoned) yields, as in DDT poisoning, spontaneous trains of repetitive impulses.

(2) In Tenebrio pupae, injection of naphthalene in olive oil yielded same effects as exposure to vapors.

(3) By all routes slow acting; fat bodies probably first tissues affected; nerve and muscle tissues not among first affected; discolored and dying pupae are still capable of wriggling response to stimulus.

(4) Tissue oxidase systems poisoned; hemolymph darkened (red → black); dissolution of the fat body.

b) For Tenebrio larvae toxicity declined with increased age and wgt; sub-lethal exposures had no effect on subsequent growth of young larvae. 2556

c) Resistance to naphthalene varies greatly between instars of the more advanced stages of Tenebrio; order of susceptibility (greatest → least) = egg > young larva > adult > pre-pupa > pupa > mature larva. 2556

d) Among tested insects, Diptera appear most susceptible, Coleoptera most resistant. 2556

e) Toward Tribolium confusum, naphthalene is reported to be 10 to 14 times more toxic than p-dichlorobenzene at the same concentration; at naphthalene saturation (0.0000067 moles/l) the approximate LT_{50} (exposure time for 50% kill) lies between 6 to 6.5 hours (40.7% kill at 6 hr. exposure, 60.7% at 6.5 hr. exposure, 92.7% at 9 hr. exposure). 1956

f) The length of exposure to kill Popillia japonica (larva) in a naphthalene saturated atmosphere varies with temperature; 12 hrs. exposure required at 80°F, 120 hrs. exposure at 50°F. Mortality varies directly with relative humidity. Order of resistance: Larva < egg < pupa. 1028

g) Development of clothes moth eggs is inhibited by naphthalene in enclosed spaces at room temperatures; no hatch after 14 day exposures. 1503

h) Toxic to eggs of Tetranychus bimaculatus; 8 hrs. exposure at saturation was required to suppress hatching; a slight resistance increase between larva and adult was noted. 1433 2586

i) Periplaneta americana and Musca domestica, exposed to vapors produced by spraying naphthalene in o-dichlorobenzene (30g/100cc) on a hot surface (375°C): All Musca dead in 24 hrs; 95% of Periplaneta dead in 3 days, 99% after 10 days. 3004

5) Uses; miscellaneous data:

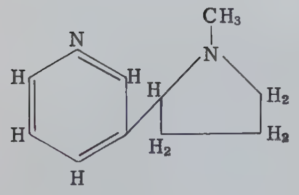
a) To control clothing insects: Tineola bisselliella, Tinea pelloniella, Anthrenus scrophulariae, Attagenus piceus, required 10 lb/100 ft^3 in ball form 5 lb/100 ft^3 in flake form. 396

b) Vs. Psila rosae in seeds: Reported to give better control than DDT or rotenone. 1203

c) Used vs. the overwintering nymphs of Eriosoma lanigerum as soil fumigant; vs. Heliothrips haemorrhoidalis (space fumigation), vs. Thrips tabaci (in dusts), vs. Psila rosae (in dusts), vs. Chrysobothris femorata (as a "paint" suspension in soap solution), vs. Tetranychus telarius (space fumigation), vs. Pediculus humanus (as an adjuvant to increase "knockdown"). 2226 353 1501

130

NICOTINE [L-1-Methyl-2-(3′-pyridyl)-pyrrolidine; β-Pyridyl-α-N-methylpyrrolidine; Pyridyl-N-methylpyrrolidine; 1-3-(1-Methyl-2-pyrrolidyl) pyridine.]



Molecular weight 162.23

GENERAL

(Also consult Anabasine; Nornicotine)
[Refs.: 353,2231,2120,129,2815,1059,757,1377,2504,2221,1664,1221,851,1484,1580,2664,2665,2108, 1801,2662,2538,977,539,3261,825,3056,1801,1782]

One of the most important of all insecticides, and one of the several natural plant products employed in insect control. The insecticidal powers of tobacco extracts have long been recognized and the active insecticidal alkaloids (of which nicotine is one) have been isolated and long since synthesized. Intensely toxic to mammals (and, indeed, to all vertebrates) by ingestion, inhalation, parenteral and dermal application. Highly toxic to most insects by contact and fumigant action and, in the form of its salts, by ingestion. Being volatile, the contact and fumigant residual effectiveness of nicotine is limited, this being perhaps the only flaw of this exceptional insect toxicant. In its fixed forms, for instance, reineckate, silicotungstate, cuprocyanide, etc., more persistent and useful as a stomach poison. As a contact poison most effective as a soap (laurate, oleate, naphthenate). Possesses marked insect ovicidal properties. The alkaloid nicotine occurs primarily in plants of the genus Nicotiana (Solanaceae) (some 15 species) but on a commercial scale is derived chiefly from Nicotiana tabacum (2-5% nicotine in the leaves) and Nicotiana rustica (5-14% in the leaves); plant parts other than leaves possess far less alkaloid. Nicotine is known also from Aesclepias syriaca and Duboisia hopwoodi. Distillation with steam after alkali-treatment, or extraction of plant material with petroleum ether, ether, trichloroethylene or benzene, serve to free the alkaloid. Nicotine finds its most effective employment vs. soft-bodied and sucking insects such as aphids, mealy bugs, etc. Has long enjoyed universal use as the sulfate, popularly known as Black Leaf 40.

PHYSICAL, CHEMICAL

Freshly distilled: A colorless, virtually odorless, viscous liquid which, on exposure to air, darkens, increases in viscosity and acquires a characteristic unpleasant smell; b.p. 247°C (with partial decomposition); m.p. $<$-80°C; $d_{4°}^{20°}$ 1.00925; $n_D^{20°}$ 1.528; $[\alpha]_D^{20°}$- 166.39-168.5; v.p. 0.08 mmHg at 20°C, 0.0425 at 25°C, 2.8 at 80°C, 7.0 at 100°C; volatile with steam; miscible with water at temperatures $<$60°C and $>$210°C; soluble in most organic solvents and miscible with alcohol, ether, chloroform; the predominant component of the crude natural product is laevo-nicotine but related nornicotine (q.v.) and anabasine (q.v.) may be present; basic in nature, nicotine readily forms salts (usually water-soluble) with acids, dibasic salts, metals. So-called "fixed" forms, such as the reineckate, silicotungstate, cuprocyanide, are water insoluble salts; the sulfate is the form in commonest insecticidal use; 0.04 lb will saturate, as vapor, 1000 ft^3 of air at 68°F; one of the most virulent of poisons; related alkaloids present in tobacco, beside those already mentioned, include: nicotimine, N-methylanabasine, isonicoteine, anatabine, 1-N-methylanatabine, nicotyrine, nicotelline, 2,3-dipyridyl, nicoteine.

a) Formulations: Concentrates for dilution as sprays, for example crude alkaloid 95%, nicotine sulfate 40% (soap or alkali being needed to liberate nicotine; 3-5% dusts; impregnated papers etc., for fumigation uses. Chlorination of the alkaloid with chlorine gas does not affect toxicity for aphids.

b) Maximum amount of nicotine which can exist as a vapor in a 1000 ft^3 fumigation chamber at various temperatures: 2671

Temperature (°F)	V.P. (mmHg)	As Vapor Lbs/1000 ft^3
68	.08	.04
77	.12	.07
86	.16	.09
95	.23	.12
104	.30	.16
113	.41	.22
122	.55	.28

TOXICOLOGICAL

1) Toxicity for higher animals:
   - a) One of the most deadly and rapidly acting poisons known, with a primary action on the nervous system which is first stimulated then depressed with ultimate paralysis and functional failure of organs. The toxicity for the animal kingdom increases with the neural complexity of the organism. Intensely toxic to mammals by inhalation or dermal application being rapidly absorbed via the skin. Absorbed more rapidly via the tongue or the eye than via the stomach. Symptoms of intoxication have appeared in spray workers using 0.1% nicotine solutions. Base more readily absorbed via skin than the salts. 1221,2159 968,1336 1918,1212 2221,353 2900,1949 1270
   - b) For Man: The MLD is ca. 60 mg/individual, and 4 mg may give rise to grave symptoms.
   - c) For the Cat: 1.2g cutaneously applied are rapidly fatal.
   - d) The hazard, unless the toxicity is made clearly apparent and precautions taken, may be very great.
   - e) For animals generally (vertebrates) the lethal dose (oral) = ca. 10 mg/k.
   - f) Symptoms of intoxication, Man: 2231
     - (1) Symptoms are rapid in onset and include: Headache, vertigo, nausea with vomiting, visual disturbances, hearing disturbances, mental confusion, asthenia, rapid respiration, faintness, prostration, convulsions, and finally, death by respiratory failure.
     - (2) Parpanit intravenously at 20-30 mg/k suppresses toxic action. Dipparcol intravenously at 15-30 mg/k protects against lethal doses. 1518,1517 1516
   - g) Spray residues present little hazard, being volatile and evanescent; fixed nicotines present a potential hazard. 2231

2) Acute toxicity; higher animals: (Once central medullary paralysis has begun, death is inevitable [Ref. 1221]
   - a) Unless specifically indicated, dosages may be in the form of nicotine base (alkaloid) or of nicotine salt(s).

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	MLD	24		1506
Mouse	sc	MLD	16		1506
Mouse	iv	MLD	0.8		530
Mouse	iv	LD$_{50}$	7.1		1923
Rat	or	LD$_{50}$	50-60		1951
Rat	sc	LD$_{60}$	33.5		210
Rat	iv	MLD	1		530
Guinea Pig	sc	MLD	15	Small animals.	1448
Guinea Pig	sc	MLD	40	Large animals.	1448
Guinea Pig	sc	LD$_{50}$	26		1319
Guinea Pig	iv	MLD	4.5		530
Rabbit	ct	LD	50-60		802
Rabbit	ct	LD$_{50}$	50	Single application.	1952
Rabbit	sc	LD	20		1448
Rabbit	iv	MLD	30-45		1039
Rabbit	iv	LD$_{50}$	9.4		1923
Dog	iv	LD$_{50}$	5.0		1923
Dog	iv	LD	3		1055
Pigeon	sc	LD	4.6		1039
Fish	Medium	Toxic	3.3-20 ppm	More toxic in alkaline than in acid sol.	2717

Specifically as the base:

Frog	sc	LD	40	2413
Rat	sc	LD	50-60	2413
Rat	or	LD$_{50}$	ca 50-60	1951
Rabbit	ct	LD$_{50}$	50	1952
Cat	iv	LD	6.1	2064

As α-nicotine

Frog	sc	LD	600	2413
Rat	sc	LD	320-640	2413
Cat	iv	LD	6.1	2064

As d-nicotine HCl

Rat	ip	MLD	23.5	1521
Guinea Pig	ip	MLD	33	1521

As l-nicotine HCl

Mouse	ip	MLD	10	1921
Rat	ip	MLD	20-23.5	1521
Guinea Pig	ip	MLD	32	1521
Rabbit	iv	MLD	6.5	1921

3) Chronic toxicity:
- a) Lowest level in diet which produced overt effects in Rats in 43 weeks exposure = 60 ppm. 1949
- b) Nicotine SO_4 in diet at 60 ppm inhibited growth of Rats; at 500 ppm 100% mortality. 3328
- c) Nicotine bentonite, nicotine tannate at 1000 ppm in diet fatal to Rats. 3328
- d) Habituation may be established to sub-lethal dosages. Tolerance develops on repeated administration. 3328,1221

4) Pharmacological, pharmacodynamic, physiological etc.; higher animals: 1221
- a) Dextro- and laevo- forms appear to have same potency.
- b) Mode of action:
  - (1) Primary transient stimulation, then a longer lasting depression of all sympathetic and para-sympathetic ganglia.
  - (2) Action is direct on the ganglionic neurons.
  - (3) During initial excitation preganglionic impulses are more effective; in phase of paralysis pre-ganglionic impulses are wholly ineffective.
  - (4) Post-ganglionic response is unimpaired.
  - (5) No influence on acetylcholine release in ganglia by cholinergic preganglionic impulses; renders ganglionic cells more sensitive then more resistant to acetylcholine.
  - (6) Effects on skeletal muscle resemble effects on ganglia; in stage of paralysis the action is curare-like (thus respiratory paralysis). Nicotine is, however, unlike curare more active on ganglia than on striated muscle.
  - (7) Initial stimulation is attended by ganglion cell depolarization which subsequently prevents transmission by competitive acetylcholine blockade.
  - (8) CNS and other effects: Initial stimulation followed by neuronal paralysis; evidence also of direct action on non-striated muscle elements of blood vessels with vaso-constriction; increases intestinal motility.
- c) The pharmacologically complex action of nicotine is associated in part with the stimulant and depressant action phases. On the surface the effects may be apparently paradoxical. For details consult Refs.: 1221, 851. Direct effects on the adrenal medulla are worthy of mention as adding to the pharmacologic complexity of nicotine action.
- d) Metabolic fate: 3284,1221
  - (1) 80-90% of intaken nicotine is chemically altered mainly by liver, also by kidney and lung. Undetoxified fractions are eliminated via urine with altered fractions. 3283 3285
  - (2) Excretion rate is rapid and increases as the dose, with elimination even of large doses complete in ca. 16 hours. Urine alkalinity slows final excretion (reabsorption of alkaline base by the nephron). Excreted in milk of lactating females. Nicotyrine is the principal detoxification product; no nicotine oxide, nicotinic acid or nicotinic acid amide or pyridine have been identified.

5) Phytotoxicity:
- a) Under all ordinary circumstances and at insecticidal dosages, non-toxic to plants. 353
  - (1) As a fumigant at high concentrations, reported to have damaged potato foliage. Violets are reported susceptible to nicotine damage in fumigation; alkalinity of nicotine is a possible explanation of toxic effect.

6) Toxicity to insects: [Refs.: 45,262,1604,2608,2627,2814,2904,2621,2483,3056]
- a) Relation of administration route to nicotine toxicity: 206

Route	LD_{50} ($\mu g/g$)				LD_{95} ($\mu g/g$)			
	Apis mellifera	Popillia japonica	Onco-peltus fasciatus	Galleria mellonella	Apis	Popillia	Onco-peltus	Galleria
Parenteral	52	738	36	843	37.8 mg/g	84.74 mg/g	407	3818
Enteral	–	532	–	742	–	31.9 mg/g	–	6972
Topical	315	890	105	22.8 mg/g	935	15.15 mg/g	292	584 mg/g
Fumigant	708	+*	43	+	7320	+	146	+

*=Beyond measurable quantity; in excess of maximum measurable dose.

- (1) Toxicity of nicotine (free alkaloid) for several insect species, based on work and methods of a single investigator: 2219

Insect	Route	Dosage ($\mu g/g$) For Mortality			Insect Weight (g)
		0% Mortality	50% Mortality	100% Mortality	
Anasa tristis	Topical	150	350	1250	.126 (.08-.16)
" "	Injection (blood)	50	200	350	
Bombyx mori (larva)	Topical	0.6	4	8	1.2 (.6-1.9)
" " "	Injection (blood)	0.5	3	7	
Ceratomia catalpae (larva)	Topical	40	100	200	1.5 (1-2.3)
" " "	Injection (blood)	40	80	150	
Oncopeltus fasciatus	Topical	90	190	450	.065 (.04-.09)
Periplaneta americana	Oral	♂900, ♀2000	♂2400, ♀3100	♂4000, ♀5200	.9 (.7-1.15♂)
" "	Topical	80, 650	140, 800	500, 1300	1.3 (1-1.9♀)
" "	Injection (blood)	30, 80	80, 120	140, 200	

(1) Toxicity of nicotine (free alkaloid) for several insect species, based on work and methods of a single investigator: 2219

Insect	Route	Dosage (µg/g) For Mortality			Insect Weight (g)
		0% Mortality	50% Mortality	100% Mortality	
Popillia japonica	Topical	300	650	1000	.096 (.07-.14)
" "	Injection (blood)	150	400	900	
Tenebrio molitor	Topical	2000	3200	4400	.105 (.08-.15)

(2) Toxicity of nicotine as a fumigant; air flow fumigation at 77°F (25°C) flask fumigation at ca. 0% relative humidity; mortality counts mainly at 24 hrs. post-exposure, (nicotine saturation = 0.278 mg/l): 2628

Insect	Stage	Exposure (Min.)	Approximate Concentration (mg/l) For	
			50% Mortality (LC_{50})	95% Mortality (LC_{95})
Eriosoma americanum	adult	3	<.003	—
" "	"	7.5	<.003	—
Aphis gossypii	"	30	.0032	.0039
Macrosiphoniella sanborni	"	30	.0037; .0077	.004; .0091
Aphis rumicis	"	1	.011	.025
" "	"	30	.0038; .0054	.0042; .0059
Aphis forbesii	"	30	.0048	.0058
Myzus solanifolii	"	30	.0063	.0070
Macrosiphum pisi	"	1	.049	.07
" "	"	7.5	.015	—
" "	"	30	.008	.013
Myzus porosus	"	30	.0095	.012
Brevicoryne brassicae	"	1	.074	.122
" "	"	7.5	.020	.036
" "	"	30	.01	.016
" "	"	90	.007	.0085
Myzus persicae (on turnip, lettuce)	"	30	.013	.018
" " (on dahlia)	"	30	.0072	.0087
" " (on nasturtium)	"	7.5	.0067	.012
" " "	"	30	.004	.0062
" " "	"	90	.003	—
Trialeurodes packardi	"	30	.0085	.012
T. vaporariorum	"	30	.014	.027
Empoasca fabae	"	30	.0094	.018
Orthezia insignis	"	30	.027	.041
Phenococcus gossypii	"	30	.150	.200
Carpocapsa pomonella	"	3	.020	.038
" "	"	7.5	.012	.020
" "	"	30	.0045	<.008
" "	1st instar	30	.014	.023
Bombyx mori	2nd instar	30	.0068	.0081
" "	6th "	30	.0085	<.011
Phlyctaenia rubigallis	adult	30	<.015	—
" "	5th instar	30	>.278	—
Heliothis armigera	1st "	30	<.030	—
" "	6th "	30	>.278	—
Prodenia eridania (unfed)	1st "	30	.010	—
" " (on Ricinus)	2nd "	30	.035	.055
" " (on sweet potato)	1st "	30	.016	.025
" " "	4th "	30	.210	—
" " (on Ricinus)	6th "	30	>.271	—
Bregmatothrips iridis	adult	30	—	<.013
Thrips tabaci	"	30	.0075	.020
Taeniothrips simplex	"	30	.010	.019
" "	larva	30	.016	.026
Heliothrips femoralis	adult	30	.018	.027
Thrips nigropilosus	"	30	.060	.067
" "	larva	30	—	<.028
Diabrotica vittata	adult	30	>.06	—
Epitrix parvula	"	30	.095	.150
Epicauta pennsylvanica	"	4	.278	—
" "	"	12	—	.278
Epilachna varivestis	"	30	.145	.250
Popillia japonica	"	110	.278	—

(2) Toxicity of nicotine as a fumigant; air flow fumigation at 77°F (25°C) flask fumigation at ca. 0% relative humidity; mortality counts mainly at 24 hrs. post-exposure, (nicotine saturation = 0.278 mg/l): 2628

Insect	Stage	Exposure (Min.)	Approximate Concentration (mg/l) For 50% Mortality (LC$_{50}$)	95% Mortality (LC$_{95}$)
Tribolium confusum	adult	140	.278	—
" "	"	300	.278	—
Aphidius phorodontis	adult	7.5	<.0060	.0080
Reticulitermes flavipes	adult worker	30	.0075	.010
Tetranychus bimaculatus	adult	30	.085	.150
Musca domestica	"	30	.120	.190
Periplaneta americana	"	30	>.150	<.170
Apis mellifera	"	60	>.244	—
" "	"	90	—	<.259

a) In the above data the following may be noted with respect to vapor toxicity of nicotine for insects:
   (1) Wide species variation in susceptibility.
   (2) Particular susceptibility of aphids, some thrips.
   (3) Rapid action.
   (4) Marked differences in some insects depending on host plant e.g. Myzus persicae.
   (5) " " " " " " " life cycle stage.
   (6) Short exposures to high concentrations more effective than proportionately long exposures at low concentrations.
   (7) Concentration influences effectiveness more than exposure time.
   (8) For some insects, more toxic as vapor than HCN.

(3) Toxicity of nicotine for insects by various routes:

Insect	Route	Dose	Dosage	Remarks	
Anthonomus grandis	Fumig	LD	ca 19 µg/g		3216
Aphis rumicis	Contact	LD$_{50}$	48 µg/g		2836
Aphis rumicis	Contact	LD$_{80}$	115 µg/g		2836
Aphis ?	Contact Spray	LC$_{95}$	0.01%		2613
Apis mellifera (adult)	Topical	LD$_{50}$	315 µg/g		206
Apis mellifera (")	Inj.	LD$_{50}$	52 µg/g		206
Blattella germanica	Contact	LD$_{50}$	2150 µg/g		2836
Blattella germanica	Contact	LD$_{80}$	3200 µg/g		2836
Bombyx mori (larva)	sc	LD	1440 µg/g		2188
Calliphora erythrocephala ♂	sc	LD	1080 µg/g		2188
Calliphora erythrocephala ♀	sc	LD	1090 µg/g		2188
Bombyx mori (larva)	or	MLD	3.5 µg/g	Leaf sandwich method; alkaloid.	1378
Carpocapsa pomonella	sc	LD	850 µg/g		2188
Choristoneura fumiferana (larva)	Contact Spray	LDeposit$_{50}$	42 µg/cm^2		350
Celerio lineata	sc	LD (estimate)	200-1000 µg/g	Given as nicotine SO$_4$.	1548
Datana integerrima (3rd instar)	or	MLD	160 µg/g	Leaf sandwich method; alkaloid.	1378
Galleria mellonella	or	LD$_{50}$	742 µg/g		206
Galleria mellonella	inj	LD$_{50}$	843 µg/g		206
Galleria mellonella	Topical	LD$_{50}$	22,800 µg/g		206
Heliothis ononis	Contact Spray	LDeposit$_{50}$	400 µg/cm^2		350
Lucilia sericata ♂	sc	LD	370 µg/g		2188
Lucilia sericata ♀	sc	LD	650-690 µg/g		2188
Lygaeus kalmii	Contact	LD$_{50}$	3200 µg/g		2836
Lygaeus kalmii	Contact	LD$_{80}$	6800 µg/g		2836
Oncopeltus fasciatus ♂	Contact	LD$_{50}$ 6 day	200 µg/g		2822
Oncopeltus fasciatus ♀	Contact	LD$_{50}$ 6 day	230 µg/g		2822
Periplaneta americana	Absorbed Vapor	LD$_{50}$	1200 µg/g		1204
Phormia regina (larva)	sc	LD	3310 µg/g		2188
Prodenia eridania (larva)	sc	LD	1980 µg/g		2188
Protoparce quinquemaculata	or	MLD	3530 µg/g	Leaf sandwich method; alkaloid.	1378
Thermobia domestica	Contact Spray	LC$_{50}$	270 mg/100cc ± 20		1814
Thermobia domestica	Contact Spray	LC$_{100}$	(ca) 400-500 mg/100cc		1814
Tribolium castaneum	Contact Spray	LC$_{50}$	0.29% →	alkaloid in 20% v/v acetone + .1% lorol as the reineckate; non-repellent in the solution fed at 0.5 g/100cc.	2532
Rhagoletis pomonella (adult)	or	LD$_{50}$ 24 hr	7.9 µg/g		2259

(4) Toxicity of nicotine alkaloid for several insects by injection into pharynx and blood. Insects = 4th and 5th instar larvae; various Lepidoptera: 1378

Insect	Mean Wgt (g)	Dose (mg/g)	Injection Site	% Mortality
Protoparce quinquemaculata	6.2	10	Pharynx	86
" "	7.4	5	"	100
" "	10.5	3.5	"	100
" "	9.2	2	"	29
" "	8.8	1	"	60
" "	9.3	(control) H$_2$O	"	0
" "	7.2	2.5	Blood	60
" "	7.5	.5	"	0
" "	10.3	.1	"	0

(4) Toxicity of nicotine alkaloid for several insects by injection into pharynx and blood. Insects = 4th and 5th instar larvae; various Lepidoptera: 1378

Insect	Mean Wgt (g)	Dose (mg/g)	Injection Site	% Mortality
Pieris rapae	0.16	5	Blood	100
" "	.16	2	"	80
" "	.14	1	"	30
" "	.165	(control, H_2O)	"	0
Hyphantria cunea	.225	2.5	Pharynx	0
" "	.1	1	"	0
" "	.18	.1	"	0
" "	.07	2.5	Blood	0
" "	.07	1	"	0
" "	.24	.1	"	0
Carpocapsa pomonella	.042	1	Pharynx	0
" "	.043	.1	"	0
Bombyx mori	.59	.004	"	100
" "	.6	.0025	"	80
" "	.54	.002	"	40
" "	.42	.0015	"	30
" "	.46	.004	Blood	100
" "	.41	.0025	"	70
" "	.42	.0015	"	30
" "	.25	.0025	Pharynx	20
" "	.25	.002	"	20
" "	.25	.0015	"	20
" "	.28	.001	"	0
" "	.25	.0005	"	0
" "	.41	.0025	Blood	80
" "	.35	.002	"	40
" "	.39	.0015	"	40
" "	.32	.001	"	20
" "	.31	.0005	"	0

(5) Toxicity of nicotine alkaloid fed to various insects by the leaf sandwich method; insects = 4th, 5th instar larvae unless otherwise stated: 1378

Insect	Mean Wgt (g)	Maximum Non-Lethal Dose (μg/g)	Remarks
Malacosoma americanum	.29	414	
Hyphantria cunea	.23	1020	
Lycophotia margaritosa saucia	.545	2070	
Mamestra picta	.74	460	
Estigmene acraea	.88	560	
Halisidota caryae	.07	160	
Protoparce sexta	.84	7080	
Protoparce quinquemaculata	3.9	3830	MLD = 3530 μg/g
Cacoecia cerasivorana	.03	54	
Leptinotarsa decemlineata (adult)	.15	570	
" " (larva)	.083	1010	
Pieris rapae	.12	3640	
Datana integerrima (3rd instar)	.15	95	MLD = 16 μg/g
" " (5th instar)	.33	120	MLD = 13 μg/g
Bombyx mori	.13	13	MLD = 3.5 μg/g

(6) Toxicity of various nicotine compounds fed to certain insects by the leaf sandwich method; 4th, 5th instar larvae unless otherwise indicated: 1378

Insect	Nicotine Compound	Max. Non-Lethal Dose (μg/g)	MLD (μg/g)
Halisidota caryae	reineckate	200	
Protoparce quinquemaculata	reineckate	170	18
Cacoecia cerasivorana	caseinate	49	
" "	peat	186	
" "	$SnCl_2$	1020	
" "	reineckate	79	
Pieris rapae	reineckate	1780	
" "	aresket	9800	
" "	2,4-dinitro-o-cyclohexylphenate	720	13

(6) Toxicity of various nicotine compounds fed to certain insects by the leaf sandwich method; 4th, 5th instar larvae unless otherwise indicated: 1378

Insect	Nicotine Compound	Max. Non-lethal Dose (μg/g)	MLD (μg/g)	
Datana integerrima	reineckate	35		
Bombyx mori	reineckate	17	2.5	
" "	silicotungstate	16	10	
Leptinotarsa decemlineata	reineckate	68	11	
" "	silicotungstate	95	8.7	
Leptinotarsa decemlineata (adult)	reineckate	8	4	
" " "	silicotungstate	57		
Rhagoletis pomonella (adult)	peat } oral	non-toxic in amounts accepted by insects.		2259
Rhagoletis fausta (adult)	peat			
Rhagoletis pomonella (adult)	bentonite oral	no mortality at the amounts accepted.		2259
Rhagoletis pomonella (adult)	silicotungstate	1400 μg/insect, oral, of a 36 mg/cc solution non-toxic.		2259

(7) Toxicity of nicotine alkaloid and nicotine compounds as sprays vs. Aphis rumicis; concentrations given are those showing highest mortality in the tests: 2388

Nicotine Compound	Conc. (% Actual Nicotine)	Mortality (%)	Nicotine Compound	Conc.(% Actual Nicotine)	Mortality (%)
Alginate	0.5	100	Silicotungstate	0.5	0
Aresket	.6	100	Reineckate	.05, .5	1
Caseinate	.5	100	Resorcinol-formaldehyde	.5	5
Humate	.5	100	Cuprocyanide	.5	11
$CuCl_2$ double salt	.1	30	Alkaloid + 1% saponin	.2	83
$ZnCl_2$ " "	.1	30	" + 25% Na oleate	.2	100
$SnCl_2$ " "	.1	52	Dodecyl nicotinium iodide	.5	83
Laurate	.1	100	" " diiodide	.5	72
Oleate	.07, .1	100	" " bromide	.5	80
Linoleate	.07, .1	100	" " dibromide	.5	70
Stearate	.1	98			
Naphthenate	.1	100			
Bentonite	.5	52			

(8) Toxicity of fixed nicotine preparations for lepidopterous larvae, crawling and/or feeding on leaves dusted with test compounds: 3035

Material	Dust mg/in^2	% Mortality In									
		Cabbage worm		Diamond back moth		Green Cutworm		So. Armyworm		Greenhouse Leaf Tier	
		2 days	4 days	2 days	4 days	2 days	4 days	2 days	5 days	2 days	5 days
Nicotine tannate-clay	0.4	47	97	82	100	60	100	2	22	0	7
	.5	35	55	95	100	85	100	0	5	3	7
	.8	62	97	92	100	90	100	0	27	0	5
	1.0	90	100					0	32	2	13
Nicotine-clay + ammonium-sulfo soap	.2	20	72	86	95	95	100	0	0	0	13
	.3			84	100	95	100	0	0	8	8
	.4	90	100	100	100	100	100				
	.6										
	.7							16	20	2	5
	.8							12	25	12	17
	1.0							12	30	16	29
	1.5							85	96	48	54
Nicotine-bentonite + ammonium-sulfo soap	.2	36	95	100	100	60	95	5	5	5	25
	.4	10	95	100	100	100	100	0	39	2	10
	.6			100	100	50	100				
	.7	15	80	100	100	90	100	2	7	5	25
Nicotine-bentonite	0.2	82	82	90	100	100	100				
	.3	77	97	100	100	93	100	0	21	7	39
	.5	100	100	100	100	100	100	0	42	8	50
	1.2							84	92	8	54
Nicotine silicotungstate	.2	65	100	90	100	73	100		—	7	44
	.3	85	100	100	100	90	100	51	100	5	25
	.5	95	100			50	100	66	100	3	88
	.8							100	100	65	100

(8) Toxicity of fixed nicotine preparations for lepidopterous larvae, crawling and/or feeding on leaves dusted with test compounds (Continued): 3035

Material	Dust mg/in^2	% Mortality In									
		Cabbage worm		Diamond back moth		Green Cutworm		So. Armyworm		Greenhouse Leaf Tier	
		2 days	4 days	2 days	4 days	2 days	4 days	2 days	5 days	2 days	5 days
Nicotine bitartrate	.2	57	95	100	100	100	100	11	16	25	35
	.4	80	100					37	51	52	85
	.7	80	100					88	100	92	100
	.9									100	100

7) Comparative toxicity, nicotine and other compounds for insects:

a) Nicotines, nornicotines, anabasine vs. Aphis rumicis; as sprays: 2606, 1376

Compound	Vs. Adult Wingless ♀♀		Mean Mortality (%) At Concentration					
	LC$_{50}$ (mg/100cc)	LC$_{100}$ (mg/100cc)	.005%	.02%	.05%	.2%	.4%	2.0%
l-β-Nicotine	49	1,185	8	32	80	87	100	—
d-β-Nicotine	—	—	—	—	28	45	90	100
dl-β-Nicotine	96	1,259	—	—	—	—	—	—
dl-α-Nicotine	1496	10,960	—	—	—	—	—	—
l-β-Nornicotine	—	—	16	63	98	100	—	—
d-β-Nornicotine	—	—	16	45	65	100	—	—
dl-β-Nornicotine	45	490	13	37	90	100	—	—
dl-α-Nornicotine	1514	10,470	—	—	—	—	—	—
Anabasine	5	166	—	—	—	—	—	—

b) Toxicity and dissociation constant of substituted pyrrolidines for insects: 353,2613,632

Compound	Tribolium LC$_{50}$ mg/l Vapors	Aphis LC$_{95}$ (% conc) Spray	Dissociation Constant pK
β-Nicotine	0.03	0.01	6.95
α-Phenylpyrrolidine	.24	.5	4.4
N-Butylpyrrolidine	1.7	.5	3.64
N-Methylpyrrolidine	9.5	1.0	3.82
Pyrrolidine	1.1	1.0	2.89

c) Nicotine and other insecticides, vs. Aphis rumicis (adult) as contact sprays: 2952

Compound	Concentration (As Base) g/100 cc	Net Mortality (%)	
		Average	Range
l-Nicotine*	0.02	13	13- 13
	.03	55	32- 89
	.04	69	35- 89
	.05	77	77- 77
	.08	93	89-100
l-Nicotine acid δ-tartrate	.02	32	18- 45
	.03	59	29- 80
	.04	87	80-100
	.06	94	90-100
l-α-p-Tolylpyrrolidine acid l-tartrate	.6	1	0- 20
	1.2	11	0- 32
	1.5	65	49- 80
	1.8	90	80-100
	2.4	100	100
d-α-p-Tolylpyrrolidine acid d-tartrate	.6	6	0- 10
	1.0	35	8- 69
	1.2	51	36- 68
	1.45	64	32-100
	1.8	47	36- 57
	2.4	58	33-100

*dl-Nicotine ca. 0.5 times as toxic as l-Nicotine.

d) Toxicity of α-substituted pyrrolines and pyrrolidines, to Thermobia domestica, an insect showing relative resistance to many toxicants; as contact sprays: 1814

Compound**	LC$_{50}$ (g/100cc)	LC$_{100}$ (approx) (g/100cc)
1-β-Nicotine	0.27 ± .02*	0.4-0.5
2-Mesityl-α-pyrroline	.84 ± .1	ca2
2-Mesityl-α-pyrrolidine	.97 ± .07	ca2

d) Toxicity of α-substituted pyrrolines and pyrrolidines, to *Thermobia domestica*, an insect showing relative resistance to many toxicants; as contact sprays (Continued): 1814

Compound**	LC$_{50}$ (g/100cc)	LC$_{100}$ (approx) (g/100cc)
l-α-Cyclohexyl pyrrolidine	1.0 ± .1	ca3.5
α-Cyclohexyl pyrroline	1.08 ± .1	"4
α-Thienyl-α-pyrrolidine	1.22 ± .08	"2
l-α-Phenyl pyrrolidine	1.31 ± .09	"4
d-α-Phenyl pyrrolidine	1.33 ± .09	"4
α-n-Butyl pyrroline	1.36 ± .17	"4
α-Phenyl pyrroline	1.37 ± .21	"3
α-Thienyl-α-pyrroline	1.39 ± .16	> 2 which = LC$_{74}$
dl-α-Cyclohexyl pyrrolidine	1.46 ± .16	ca8
α-n-Butyl pyrrolidine	1.92 ± .15	"4
dl-α-Phenyl pyrrolidine	1.99 ± 1.3	"4

*Limits (1.96 x standard error of LC$_{50}$) correspond to odds of 19 in 20.
**Physiological action of each is strongly nicotine-like.

e) Contact toxicity of nicotine and other compounds as sprays vs. 3 lepidopterous larvae: 350

Insecticide	Lethal Deposit$_{50}$ (μg/cm^2) For		
	Choristoneura fumiferana	*Heliothis ononis*	*Agrotis orthogonia*
Nicotine	42	400	Negative
Pyrethrins	0.05	4	8.2
DDT	.3	7	80
Lindane	1.9	23	5.5
Chlordane	140	Negative	18
DNOC	4	16	7.5

f) Comparative effectiveness nicotine and other compounds for control of Aphids: 353

Aphid	Order of Descending Toxicity
Aphis gossypii	parathion > nicotine, BHC, toxaphene > DDT
Brevicoryne brassicae	parathion > HETP > nicotine > DDT
Rhopalosiphum pseudobrassicae	parathion > BHC > nicotine > DDT
Macrosiphum onobrychis	parathion > HETP, BHC > nicotine, DDT, rotenone
Macrosiphum solanifolii	DDT, BHC > nicotine, rotenone
Myzus persicae	parathion > HETP > BHC > nicotine > DDT
Eriosoma lanigerum	parathion > BHC > nicotine > HETP > DDT

g) Speed of toxic action, nicotine and other compounds vs. *Macrosiphum pisi* on *Vicia faba* plants; as dusts (in talc) applied in a dusting tower: 520

Insecticide	Dust Conc (%)	Temp (°F)	Time (Hrs:Min) For	
			50% Kill	98% Kill
Nicotine	1	72	0:15	1:12
"	3	72	0:12	0:50
TEPP	0.18	74	0:20	0:56
Rotenone	5	72	0:47	1:23
Lindane	1	72	0:56	1:54
DDT	5	72	0:57	1:45
Parathion	1	70	1:8	1:43
"	2	70	1:21	1:53
Methoxychlor	10	75	2:1	5:34
DDD	5	72	2:34	4:35
Aldrin	1	75	3:44	7:32
Dieldrin	1	75	4:7	6:43
EPN	0.86	74	5:26	8:6
Chlordane	5	72	9:24	18:8
Toxaphene®	5	72	13:20	19:1
Talc (alone) control		67-72	13:28	23.51

8) Systemic action of nicotine:

a) At 0.001-0.01% concentrations nicotine and its salts are taken from solution and into the tissues of *Vicia faba*. These become toxic for *Aphis fabae* and *Pieris brassicae* (larvae). 702
   (1) Nicotine is recoverable from tissues of insects feeding on such plants.
   (2) No systemic uptake of nicotine solutions when applied to soil (decomposed?).

b) Applied to upper leaf surface nicotine kills aphids on the untreated side.
   (1) The toxic action at a distance is weak and frequent applications of strong solutions are required for the effect.
   (2) Leaf absorption and translocation not observed with nicotine salts.

9) Synergistic action of nicotine: 3141,3139

a) Synergism of nicotine and pyrethrum when injected into Oncopeltus fasciatus is reported.

(1) Tribolium confusum dipped in nicotine and pyrethrum successively or simultaneously undergoes an independent joint action.

(2) Application of nicotine followed later by pyrethrins (interval 0.75-6 hrs) indicates toxicity is highest with shortest interval between applications; evidences of synergism ca. 0 after 6 hrs. interval.

(3) Maximum observed synergism was 2-fold.

10) Repellency of nicotine for insects:

a) Nicotine (base) offered at concentrations of 0.0156-10 mg/cc to Rhagoletis pomonella, R. cingulata, R. fausta (adults) was repellent at even the lowest concentration. 2259

(1) Individuals imbibing small amounts recovered after violent effects and regurgitation.

(2) Nicotine-peat was non-toxic for R. pomonella, R. fausta in amounts accepted.

(3) Nicotine-bentonite was non-toxic for R. pomonella, R. fausta in amounts accepted.

b) Repellency of nicotine reineckate was much less than that of nicotine base for R. pomonella which will feed on solutions containing 500 mg/100cc and die (LD_{50}) in 24 hrs (as mean time) on intake of 7.9 μg/g body wgt.

c) If nicotine silicotungstate is presented to R. pomonella (adult) at concentration of 1.5 g/100cc, 50% mortality is registered at 96 hrs. (mean time); with nicotine bentonite at 3.0 g/100cc 50% mortality is registered at 215 hrs. (mean time); with the sucrose control 50% mortality is registered at 310 hrs. (mean time).

d) R. pomonella will not accept enough of a solution of 36 mg/cc concentration nicotine silicotungstate to poison itself.

11) Pharmacological, pharmacodynamic, physiological, etc.; insects:

a) Optical activity and toxicity: Laevo-β-nicotine (vs. Aphis rumicis) is 5 times as toxic as dextro-β- 1376
nicotine. DL-β-nornicotine = l-β-nicotine in toxicity; l-β-nornicotine, d-β-nornicotine, l-β-anabasine 2606
are more toxic than l-β-nicotine. 1128

b) Chemical structure and toxicity: Of some 44 substances chemically related to nicotine 1376,2606,2231
(l-β-nicotine), tested against Aphis rumicis by contact action, all were inferior in toxicity, 2613,2857,3056
compared to l-β-nicotine, save l-, d-, and dl-β-nornicotine and l-β-anabasine. 2952,1115

(1) The relative toxicity by way of injection does not follow the same order (in Oncopeltus fascia- 3140
tus) as the contact toxicity for Aphis rumicis in the substances so tested. 2231

(2) Nicotine sulfate is reported as 5 times less toxic (vs. Aphis rumicis) than anabasine sulfate: vs. 1115
Culex pipiens larvae; LD_{50} comparison showed nicotine 2 times more toxic than anabasine, 4.8 times 2606
more toxic than methylanabasine. DL-nicotine is reported as 2 times less toxic (vs. Aphis rumicis) 457
than dl-nornicotine. Vs. Carpocapsa pomonella nicotine is reported more effective than anabasine or 2832
nornicotine. In toxicity to several acarines and insects for example Brevicoryne brassicae, Macro- 298
siphum pisi, Nasturtium aphid, Paratetranychus citri, nicotine is = to nornicotine both of which are less toxic than anabasine; nicotine is more toxic than anabasine or nornicotine vs. Oncopeltus fasciatus; nicotine, anabasine and nornicotine are ca = in toxicity vs. Tetranychus telarius and Phlyctaenia rubigalis.

(3) Free nicotine base is more toxic than nicotinium ion in solution; speed of toxic action (vs. Culex pipiens 2614
larvae) is related directly to concentration of undissociated nicotine molecules, altho the nicotinium ion is not without toxic action as indicated by toxicity of solutions at pH 2 (with ca. complete ionization.)

(4) Nicotine base is 5-7 times more toxic at pH 5 than nicotine sulfate vs. Culex pipiens larvae; toxicity 633
increases in the case of free nicotine base as pH rises, with maximum at point of nearly complete 2614
undissociation; the dissociation involved is believed to be that of the pyrrolidine nitrogen. Similar 634
effects were noted in case of Aphis rumicis, but not in case of Tribolium confusum or Thermobia 632
domestica. 1813

c) "Fixed" nicotine; toxicity of:

(1) As stomach poisons, water-soluble salts of nicotine, viz. oleate, stearate, laurate, naphthenate proved 1377
ineffective vs. Carpocapsa pomonella; water-insoluble salts, viz., reineckate, silicotungstate, cuprocyanide, copper ferrocyanide proved highly effective.

(2) As contact insecticides vs. Aphis rumicis the effect of the above mentioned salts was reversed; water- 1380
solubles proved effective, water-insolubles ineffective.

(3) Via intraparenteral injection, soluble and insoluble nicotine salts showed no significant differences in 1378
toxic action nor did ingested and injected nicotine base show marked toxicity differences.

(4) Nicotine sulfate (like nicotine base), both as spray and vapor, increases in toxicity to aphids as the 758
pH of the solution; free nicotine is more volatile than nicotine sulfate and sprays as well as vapors 2187,2174
are reported to behave as fumigants.

d) Entrance of nicotine into the insect body:

(1) Direct penetration of, and absorption via, the cuticle is rapid and efficient; entrance also occurs 2607,1204
via the gastro-intestinal tract. 2604
Entrance of nicotine from solutions into Periplaneta americana; exposure time 16 minutes at 25°- 2604
26°C; ingestion of experimental solutions prevented; nicotine as the alkaloid 99% pure:

Nicotine Concentration (molar)	pH	Dissociation (%)	Nicotine Absorbed (mg/g) Minimum	Mean	Maximum	Effect
0.05	9.3	4	0.37	0.45	0.55	Insects moribund.
.05	6.4	96	.11	.28	.35	Insects 60% normal.
.05	2.8	>99.9	.18	.24	.30	Insects 83% normal.
324 mg/l .002	8.7	12.4	.02	.03	.05	Insects normal.
.002	5.0	99.8	.01	.02	.02	Insects normal.
.002	2.6	>99.9	.01	.01	.02	Insects normal.

Absorption from air is more rapid; at vapor concentration in air of 0.27 mg/l 0.2 mg/g absorbed in 1 hour. The intact nicotine molecule is absorbed more rapidly than nicotinium ion.

(2) Via direct injection: Molecular nicotine and nicotinium ion are = in toxicity for Periplaneta; difference 942
in toxicity on contact is dependent on cuticular permeability to the intact molecule and the nicotinium ion.

(3) In Periplaneta, the cuticle seems to concentrate and transport nicotine to the interior where it appears 2604
subsequently in all tissues.

(4) Rate of penetration (time of onset of toxic symptoms) on topical application varies with the cuticular 3299
thickness. Abrasion (with alumina) of the cuticular surface (in Rhodnius) decreases the time for onset 3300
of paralysis from 24 hrs to 20 minutes in case of aqueous solutions. Penetration is influenced by the 3298
cuticular waxes and lipids.

(5) Point of Application of Nicotine and average time for onset of convulsions in Tenebrio molitor (larva) 2405

Head	Av. Min. For Convulsions	Thorax	Av. Min. For Convulsions	Abdomen	Av. Min. For Convulsions
Antennae	2.6	Ventrum pro-meso-thorax	1.2	Ventrum I-II	10.0
Mouth Parts	13.0	Ventrum meso-meta-thorax	4.8	Ventrum II-III	—
Ventrum (head-thorax)	3.6	Ventrum metathorax-abdomen	24.4	Ventrum-anus	50.2

Application to non-sclerotized regions brings rapid onset of toxic signs; in Blattella germanica the 2405
most rapid action follows application to ventral cervical region; application to antenna tips of Blattella 2607
is ineffective; Periplaneta wings absorb nicotine vapors in lethal amounts. 2527

e) Site of action:

(1) Action is primarily on the ganglia of the insect CNS, possibly at the synapses, with excitation at low 3386
concentrations, depression and paralysis at higher concentrations. Little or no action on nerve fibers 2685
or the myoneural junction. Nicotinization of the insect brain brings on generalized tremors of the 2599
whole body which are extinguishable on beheading the treated insect. The insect nervous system 3056
resembles (pharmacologically) the mammalian autonomic system; nicotine (like eserine) stimulates 2231
action currents in isolated insect nerve but above a certain limit blocks them.

(2) Insect choline esterase(s) is (are) unaffected by nicotine; as in all phyla showing an acetylcholine 353
neurotransmission mechanism, l-nicotine is more toxic than d-nicotine for all insects studied except 1128
Drosophila. 2599

f) Physiological action:

(1) As in other typical neurotoxic agents induces a marked, rapid increase in oxygen uptake, for example, injection of 100 μg into Blattella yielded marked, steady rise in O_2 consumption from 0.8 mm^3/minute/insect to ca. 2 mm^3/minute/insect in ca. 1 hour followed by slow, steady decline until paralysis was complete and death occurred.

(2) At low concentrations, stimulates the insect heart to increased pulse rate. 3384,1862

(3) At high concentrations, stimulation is succeeded by depression (partial or complete) with paralysis in 3384
systole, (Periplaneta). In Melanoplus 0.1% nicotine base paralyzed the entire body with exception of 3381
heart; several applications of 1.0% nicotine base halted the isolated heart; recovery is possible by 691
repeated washing, even after 5 hrs; paralysis of alary muscles. 1364

(4) Applied topically, nicotine brings paralysis of appendages and peripheral parts of the Periplaneta body 588
long before the heart stops (after a long, irregular decline in rate of beat).

(5) Symptoms of nicotine intoxication: In general: Excitation, followed by convulsions giving way to paralysis 2405
before death. Onset of symptoms 10 times as rapid as in case of pyrethrins. In the excitatory phase 2574
metabolic rate may rise to 200 times the normal. 752

(a) In Bombyx, Celerio, Carpocapsa convulsions do not precede paralysis. 1548,2188

(b) In aphids, sprayed with lethal concentrations, death may come in 30 minutes preceded by narcosis, ataxia, withdrawal of proboscis, paralysis with twitching. 353

(c) Apis mellifera, poisoned by mouth, becomes inactive with ataxia, and succumbs to a paralysis spreading from posterior to anterior with twitching of legs and abdominal spasms; if ataxia does not supervene the insect may survive. 2187

(6) Nicotine and blood of insects: In Prodenia eridania exposure to vapor of nicotine at saturation (ca. .28 mg/l) had no effect on blood pH, although 7.15 mg/100cc of blood was present after 24 hr. exposure. 147

(7) Nicotine and cytochrome oxidase: At 10^{-3} and 10^{-5} M concentration nicotine is reported to stimulate in vitro cytochrome oxidase preparations of Periplaneta coxal muscle as measured by O_2 uptake in the Warburg apparatus. 2305

12) Nicotine and beneficial insects:

a) Predators and parasites of destructive insects are relatively unharmed by nicotine. 849,2039,2300
2384,2652,3246

b) Marked reduction of "populations" of predaceous thrips e.g., Haplothrips faurei have been reported as a consequence of nicotine sulfate use. 2650

c) 55% nicotine sulfate at 1 to 800 parts in water gave average kills of Hippodamia convergens as follows, depending on method: 26% (12-47%) 5% (2-8%), 5%, 6%, 20-30%; eggs 0% -.4% = average kill; first instar larvae 3% (0-20%) = average kill in 4 trials. 1450

d) Safe for Apis mellifera within a few minutes of application. 3099

13) Reports of field experiences in the control of economic insects with nicotine:

(1) Vs. *Lygidea mendax*: Effective for but DDT replaces. 729

(2) Vs. *Lygus pratensis*: Inadequate in the control of. 2226

(3) Vs. *Lygus campestris*: " " 33

(4) Vs. *Gargaphia tiliae*, *Corythuca ulmi*: 0.1% nicotine sulfate + soap controls. 1501

(5) Vs. *Philaenus leucophthalmus*: Superior to DDT in control of. 2465

(6) Vs. *Erythroneura comes*: Inferior to DDT in control of. 623

(7) Vs. *Psylla pyricola*: Controls, but rotenone superior. 353

(8) Vs. *Trialeurodes vaporariorum*: Effective, but others e.g. HETP, parathion, DDT replace. 2226

(9) Vs. *Aphis rumicis*: Nicotine dusts, nicotine sulfate superior to DDT for. 353

(10) Vs. *Aphis gossypii*: Gives adequate control of. 353

(11) Vs. *Brevicoryne brassicae*: Controls as dusts, sprays at 3 lb/acre. 2652

(12) Vs. *Hyalopterus arundinis*: Much superior to DDT in control of. 3287,751

(13) Vs. *Rhophalosiphum pseudobrassicae*, *R. prunifoliae*, *Macrosiphum onobrychis*, *Macrosiphum rosae*: Adequate control, superior to DDT. 353 751

(14) Vs. *Myzus persicae*: Ineffective at economical dosages. 353

(15) Vs. *Pentalonia* spp: Effective and = to others. 2906

(16) Vs. *Eriosoma lanigerum*: The insecticide of choice; superior to HETP. 2145

(17) Vs. *Saissettia oleae*: Inferior to DDT in control of. 305

(18) Vs. *Taeniothrips inconsequens*: Controlled by nicotine in oil emulsions. 2226

(19) Vs. *Thrips tabaci*: Nicotine sulfate yielded 90% control. 829

(20) Vs. *Rhyacionia frustrana*, *Grapholitha funebrana*: Inferior to DDT. 353,980

(21) Vs. *Pyrausta nubilalis*: Dusts containing "fixed" nicotine yielded 90% control. 33

(22) Vs. *Plutella maculipennis*: Nicotine sulfate superior to lead arsenate or calcium arsenate. 353

(23) Vs. *Lithocolletis* spp.: 0.1% nicotine sulfate sprays yielded control of. 1501

(24) Vs. *Melittia satyriniformis*: 80% control obtained with repeated sprays. 33

(25) Vs. *Zeuzera pyrina*, *Prionoxystus robiniae*, *P. macmurtrei*: Effective when injected into burrows of. 2226 1501

(26) Vs. *Hoplocampa testudinea*: Superior to DDT in control of. 3287

(27) Vs. *Fenusa pumila*, *Kaliofenusa ulmi*: 0.1% nicotine sulfate sprays control. 1501

(28) Vs. *Dacus cucurbitae*: Ineffective. 1573

(29) Vs. *Agromyza phaseoli*: DDT superior in control of. 1479

(30) Vs. *Monarthropalpus buxi*: 0.2% sprays yielded complete control. 2960

(31) Vs. *Diabrotica* spp. 0.05% nicotine sulfate sprays yielded 50-60% control. 1233

(32) Vs. *Bryobia pratensis*: Good control of, but ineffective as white oil emulsions. 1770

(33) Vs. *Tarsonemus pallidus*: Has been used to control. 3172

(34) Vs. *Boophilus decoloratus*: Ineffective. 353

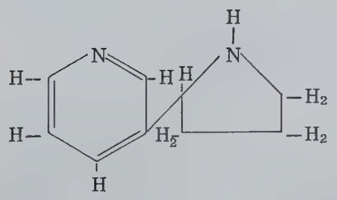
(35) Vs. *Lipeurus*, *Goniocetes*, *Menopon*, *Eumenacanthus* and various other chicken mites: DDT superior to 0.5% nicotine sprays. 3287

(36) Vs. *Thrips tabaci*: 100% kills with nicotine at 3 g/100cc, at 2 g/100cc + .25% soap; 50% kills with 0.3% nicotine + soap.

(37) Vs. *Taeniothrips simplex*: 88% kills with nicotine at 6 g/100cc; 94.8% kills at 7 g/100cc + .25% soap; 50% kills at 2.6% nicotine + soap.

131

NORNICOTINE [2-(3′-Pyridyl)-pyrrolidine; L-3(2′-Pyrrolidyl)-pyridine.]



Molecular weight 148.2

GENERAL (Also see Anabasine; Nicotine) [Refs.: 353,2231,2815,1059,757,2120,925,2522,2108,2107,313]

Nornicotine is one of the alkaloids of tobacco, possessing (as does nicotine) potent insecticidal properties. Of the alkaloid content of Nicotiana sylvestris (1%) 95% is made up of laevo-nornicotine. Dextro- and racemic-nornicotines are present in Duboisia hopwoodi which (like Nicotiana) is one of the genera of the Solanaceae. Some strains of Nicotiana tabacum have their alkaloid content mainly in the form of nornicotine (95%) with the balance as nicotine. In some commercial samples of nicotine sulfate as much as 12% of nornicotine has been found present. Essentially, nornicotine differs from nicotine in the fact that the nitrogen of the 5 membered ring is not methylated, a circumstance which does not greatly modify the insecticidal action of the molecule. Among insects the nornicotines may be considered equally as toxic as the nicotines. Among vertebrates, however, nicotine is more toxic than nornicotine for some, and nornicotine is more toxic than nicotine for others. Among the pyridyl-pyrrolidines the β,α arrangement (β-nornicotine = β-pyridyl-α-pyrrolidine) yields the most toxic isomer among the possible arrangements (α,α; β,β; γ,γ; β,α; α,β; β,γ; α,γ) being 30 times as toxic as the α,α- arrangement.

PHYSICAL, CHEMICAL [Refs.: 353,2231,2120,2221]

A colorless, viscous liquid, which on standing develops an odor less pungent than that of nicotine; b.p. 270°-271°C; $d_{4^\circ}^{20^\circ}$ 1.0737, d_{10} 1.0757; $n_D^{20^\circ}$ 1.5378, $n_D^{18^\circ}$ 1.549, $[\alpha]_D^{20} = -86.3$ (laevo-isomer); miscible with water; very soluble in alcohol, chloroform, ether, petroleum and other oils, petroleum ether, kerosene; more stable and less easily oxidized than nicotine; does not darken as readily as nicotine on exposure to air or light; less volatile than nicotine, being scarcely volatile with steam; basic (like nicotine) and forms salts readily; the natural product may occur in dextro, laevo, and racemic form; on methylation with methyl iodide yields nicotine.

a) Formulations: As in the case of nicotine, q.v.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) Although nornicotine is more toxic than nicotine for some vertebrates, and less toxic for others, the β,α-isomer of either nornicotine or nicotine is more toxic than the corresponding α,α-isomer. 353

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	ip	LD	22	As l-nornicotine.	1921
Rat	ip	MLD	6	As d-nornicotine	1521
Rat	ip	MLD	23.5	As l-nornicotine.	1521
Rat	ip	MLD	10.5	As dl-nornicotine.	1521
Guinea Pig	ip	MLD	28	As l-nornicotine.	1521
Guinea Pig	ip	MLD	10	As d-nornicotine.	1521
Rabbit	iv	LD	3	As l-nornicotine.	1921
	Comparative				
Guinea Pig	sc	LD_{50}	22	l-Anabasine.	1319,1921
Guinea Pig	sc	LD_{50}	32	l-Nicotine.	1319,1921
Guinea Pig	sc	LD_{50}	28	l-Nornicotine.	1319,1921
Guinea Pig	sc	LD_{50}	33	d-Nicotine.	1319,1921
Guinea Pig	sc	LD_{50}	10	d-Nornicotine.	1319,1921
Rat	sc	LD_{50}	23.5	d-Nicotine.	1319,1921
Rat	sc	LD_{50}	23.5	l-Nicotine.	1319,1921
Rat	sc	LD_{50}	23.5	l-Nornicotine.	1319,1921
Rat	sc	LD_{50}	6	d-Nornicotine.	1319,1921

2) Toxicity for insects:

a) Toxicity (relative) of nornicotine, nicotine, anabasine and their relatives and derivatives vs. Aphis rumicis (after Metcalf [2231] quoting the references given). Comparison based on LC_{50} values with l-β-nicotine as the standard (= 1.0). 1376,2613 2606,2857 3056,2952

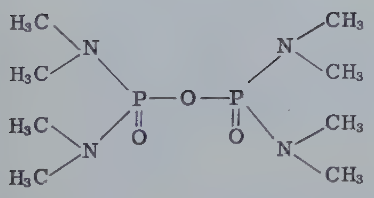
Compound	Relative LC_{50}	Compound	Relative LC_{50}
l-β-Nornicotine	0.5	Methyl-3,2'-pyridylpiperidine	20
d-β-Nornicotine	0.7	2,2'-Dipiperidyl	100
dl-β-Nornicotine	1.0	2,3'-Dipiperidyl	100
dl-α-Nornicotine	31	3,3'-Dipiperidyl	100
l-β-Nicotine	1.0	3,4'-Dipiperidyl	< 10
d-β-Nicotine	5	4,4'-Dipiperidyl	2100
dl-β-Nicotine	2	Pyrrole	> 250
dl-α-Nicotine	31	Pyrrolidine	20
l-β-Anabasine	0.1	Pyridine	125
Nicotyrine	13	Piperidine	ca 25
Metanicotine	10	α-Picoline	> 60
Dihydrometanicotine	100	Lutidine	25
Methylmetanicotine	ca 35	Quinoline	ca 10
3-Pyridyl-2-ethyl-N-ethylamine	100	Isoquinoline	ca 15
3-Pyridyl-1-n-butyl-N-methylamine	ca1600	Acridine	5
Phenyl-1-n-butyl-N-methylamine	ca1600	Benzyl pyridine	2.5
2,2'-Dipyridyl	100	Pyridyl-N-benzylchloride	ca 12
2,3'-Dipyridyl	100	L-2-p-Tolylpyrrolidine	50
3,3'-Dipyridyl	> 1000	D-2-p-Tolylpyrrolidine	40
3,4'-Dipyridyl	300		
4,4'-Dipyridyl	750		

b) Both steric isomers of β-nornicotine are equally toxic for Aphis rumicis, in contrast with β-nicotine for which the l-isomer is 10 times as toxic to Aphis rumicis, by contact, as is the d-isomer. 1376

132

OCTAMETHYL PYROPHOSPHORAMIDE

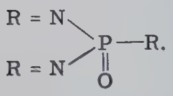
(Schradan; OMPA; Pestox III; Bis-(bis-dimethylamino) phosphonous anhydride; Octamethyltetraamidopyrophosphate; Pyrophosphoryltetrakisdimethylamide; Tetrakis dimethylamino phosphonous anhydride.)



Molecular weight 286.174

GENERAL [Refs.: 353,2231,2120,129,713,2651,649,2773,2653,858,30,3257,1695,1458,1057,493,2783,188,1801,2771 2246,1837,745,852,714,237,2867,1327,314,2538]

Octamethyl pyrophosphoramide (hereafter to be called OMPA) is one of that general group of insecticides commonly referred to as organic phosphate or "organophosphorus" insecticides. More specifically, OMPA belongs to a category referred to as phosphoramidates or pyrophosphoramide derivatives. OMPA is the only member of this category released for use, although it is not generally applicable to food crops because of danger of food contamination. OMPA is comparatively inactive as a contact insecticide but has pronounced systemic activity being taken up by the leaves of treated plants and translocated via the transpiration and sap stream to make the plant tissues poisonous to sap-feeding and chewing insects and acarines. OMPA is toxic to higher animals, although in vitro it exhibits little anti-choline esterase activity. Being apparently unable to gain access to the brain in vivo, the cholinergic action, which is acquired by conversion of OMPA in the liver (and in plant tissues) to an active choline esterase inhibiting metabolite, is mainly against peripheral tissues. OMPA, in contrast to the alkyl pyrophosphates and thiophosphates, is stable in aqueous solution. The unusual properties seem to be associated with the nitrogen-phosphorus linkage in the molecule. The general formula of the group of phosphoramidates to which OMPA belongs is:



The term Pestox III applies to a crude product which (in addition to OMPA) contains related compounds as will be described below. Regulations restrict the use of OMPA to such crops as cotton and to ornamental plants. In large scale commercial use since 1947.

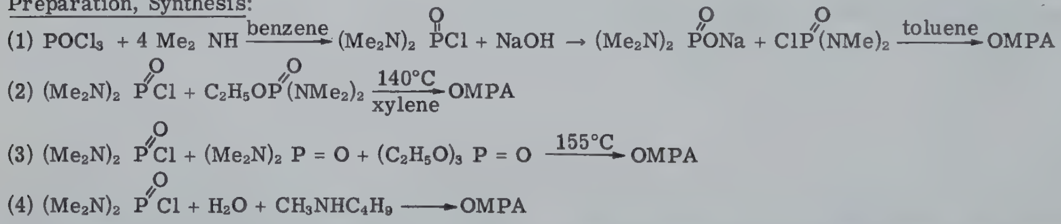
PHYSICAL, CHEMICAL [Refs.: 2651,2231,1339,2653,554,705,2773,3100,3101,1110,1416,1472,2771,1417, 2246,497]

Pure: A colorless, odorless, viscous liquid of faintly peppery taste; m.p. ca. 20°C; b.p. ca. 140°C at 2 mmHg, 120°-125°C at 0.5 mmHg, 118°-122°C at 0.3 mmHg; $d_{25°}$ 1.1343; $n_D^{25°}$ 1.4612; v.p. = 1×10^{-3} mmHg at 20°C, 2.5×10^{-4} mmHg at 25°C; vapor concentration at maximum = 2 mg/m^3; evaporation constant ca. 2×10^{-4} at 15°C; miscible with water and with most organic solvents; slightly soluble in petroleum oils, for instance spray oils; not soluble in heptane; the best extractant of OMPA from water is chloroform (partition ratio 7:1 from water at low concentration, 24:1 from low concentration in normal NaOH, overwhelmingly in favor of water in partition from vegetable, mineral oils;) hydrolyzes in acid media, the hydrolysis constants being:

$K_a = 3.6 \times 10^{-3}$ min.$^{-1}$ at 25°C (-P-N-link first)
$K_b = 4.6 \times 10^{-3}$ min.$^{-1}$ at 100°C (-P-O-P-link only)
$K_w = < 10^{-8}$ min.$^{-1}$ at 100°C;

the half-life is more than 3 years at pH4, more than 30 years at pH5-10, at 25° the half-life in 1 Normal acid = 200 minutes, 1 Normal alkali = 70 days, in neutral water 100 years. The crude compound is a dark-brown, viscous liquid of spicy odor. Non-corrosive to metals; not flammable.

Preparation, Synthesis:



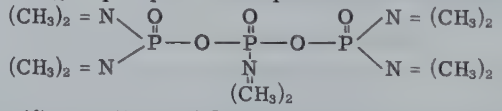
(1) $POCl_3 + 4\ Me_2NH \xrightarrow{benzene} (Me_2N)_2\overset{O}{P}Cl + NaOH \rightarrow (Me_2N)_2\overset{O}{P}ONa + Cl\overset{O}{P}(NMe)_2 \xrightarrow{toluene} OMPA$

(2) $(Me_2N)_2\overset{O}{P}Cl + C_2H_5O\overset{O}{P}(NMe_2)_2 \xrightarrow[xylene]{140°C} OMPA$

(3) $(Me_2N)_2\overset{O}{P}Cl + (Me_2N)_2P = O + (C_2H_5O)_3P = O \xrightarrow{155°C} OMPA$

(4) $(Me_2N)_2\overset{O}{P}Cl + H_2O + CH_3NHC_4H_9 \longrightarrow OMPA$

In the commercial synthesis of OMPA a complex of related compounds is formed, about 85% being phosphorus compounds extractable by chloroform from water. OMPA forms ca. 40% of the phosphorus compounds. The other major constituent is triphosphoric acid pentadimethyl amide or decamethyl triphosphoramide, also a systemic insecticide, present to 39.1% of phosphorus compounds whose formula follows:



a pale yellow, viscous liquid, specific gravity ca. 1.2, m.p. low, b.p. ca. 155°C at 2 mmHg, miscible with water and most organic solvents, partition 15:6 in favor of chloroform from water or vegetable and mineral oils; hydrolysis in acid media as follows:

$K_a = 3.5 \times 10^{-3}$ min.$^{-1}$ at 25°C
$K_b = 0.63^{-1}$ min. at 100°C
$K_w = 5 \times 10^{-4}$ min.$^{-1}$ at 100°C

half-life at 25°C and pH 4 = 2 years, at pH 6 = 2.5 years, at pH 8 = 2.5 years, at pH 10 = 2 years. A certain amount of unstable dodecamethyl tetraphosphoramide of half-life 140 seconds at 25°C in N NaOH may be present, as well as hexamethyl phosphoramide and a cyclic trimer, both of which are insecticidally inert.

a) Formulations: Aqueous solutions at 30%; anhydrous at 75% - 80%; anhydrous + wetting agent at 60%; in aerosols as a systemic agent.

TOXICOLOGICAL [Refs.: 858,1570]

1) Acute toxicity for higher animals:
   - a) Of the systemic insecticides OMPA is considered the only one really safe. 745,852
   - b) Enzymatically oxidized in vivo (or chemically by permanganate) at one of the amido-nitrogens to yield a functional group (phosphoramide N-oxide) inhibitory to choline esterase(s). 1458,858 30,1837 493
   - c) The pentadimethylamide of triphosphoric acid is reported of lower mammalian toxicity than OMPA. It is present to ca. 39% of the phosphorus compounds of technical (commercial) OMPA (Schradan). 2651 2120
   - d) Residue hazards:
     - (1) Negligible, because of restrictions governing use. 1458

e) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	30 ± 3.1		1057
Mouse (albino)	sc	LD	1.5-7		2773
Mouse	ip	LD_{50}	17		860
Mouse	ip	LD_{50}	8		860
Rat	or	LD_{50}	ca13.5	Systox 9.4; Potasan 19; malathion 1400-5834 TEPP 1.2-2; para-oxon parathion 6-15	1951,1057
Rat	or	LD_{50}	10 ←		2231
Rat ♀	or	LD_{50}	35.5 ± 3.4		1057
Rat ♂	or	LD_{50}	13.5 ± 0.34		1057
Rat	ip	LD_{50}	8-8.5		861,860
Rat	ip	LD_{100}	1.0 mg/k/day	Death to all within 10 days.	859
Guinea Pig	or	LD_{50}	15.0 ± 0.88		1057
Guinea Pig	ip	LD_{50}	10.0		860
Rat	or, sc	LD	18		2653
Rat	or	LD_{50}	8-10	As a 1% aqueous solution.	129
Rabbit	ct	LD_{50}	<780	As a 20% aqueous solution.	1952
Rabbit	or	LD_{50}	25	As a 1% aqueous solution.	129
Dog	iv	LD_{50}	5-10		860

2) Sub-acute, sub-chronic and chronic toxicity; higher animals:

a) Rats: Intraperitoneal at 0.5 mg/k/day for 60 days gave no deleterious effect; at 1.0 mg/k/day all subjects died within 10 days. 859

b) Rats: At 0.5 mg/k/day for 37 days yielded complete inhibition of erythrocyte choline esterase, at 0.1 mg/mg/k/day gave depletion of erythrocyte choline esterase to 38% of normal; at 0.02, 0.007 mg/k/day brought no response. 923

c) Rats fed for 52 weeks at: (↓ = decline) 190

10 ppm: Brain ChE ↓ to 81.5%; plasma ChE ↓ 49.7%; erythrocyte ChE ↓ 33%
3 " : Brain ChE ↓ to 93%; " " ↓ 76%; " " ↓ 45.3%
1 " : " " ↓ to 98.5%; " " ↓ 96.4%; " " ↓ 64.2% } Of Normal
0.3 ppm: Brain ChE No Effect; " " No Effect; " " ↓ 93.4%
0.1 " : " " " " ; " " " " ; " " ↓ 93.1%

(1) Markedly depressed level of whole-blood choline esterase, but not of brain choline esterase. 188

(2) Rat erythrocyte choline esterase proved particularly sensitive to OMPA; effect marked at 1 ppm OMPA in diet. 1057

d) Rats (♂) at 50 ppm in diet for 1 year: Toxic signs; growth retarded in early phases but attained normal range in the end; no pathology evident; at 10 ppm: No overt toxic signs; no pathological changes. 1458

e) Dogs, receiving 1 mg/k/day or more daily, showed severe toxic signs; prolonged feeding at 0.5 mg/k/day: Choline esterase activity of erythrocytes reduced to ca. 0, of plasma to ca. 50% of normal, without gross signs of toxicity or tissue pathology. 3144

f) Rats, exposed daily and repeatedly to concentrated vapors of OMPA: Total inhibition of erythrocyte choline esterase activity, definite inhibition of plasma choline esterase; no inhibition of brain choline esterase activity. 1458

g) 30 mg/day = upper safe therapeutic dose (man) in treatment of myasthaenia gravis. 2783

3) Pharmacological, pharmacodynamic, physiological, etc.; higher animals; Also consult the general treatment titled Organic Phosphate Insecticides:

a) The molar concentration of OMPA for 50% inhibition of choline esterase in vitro = $>1 \times 10^{-2}$ [for ethyl di-(dimethylamido) phosphate = $>1 \times 10^{-2}$; for bis-(dimethylamido) phosphorofluoridate = 4×10^{-5}; for diethyl di-(dimethylamido) pyroposphate (sym.) = 4.7×10^{-7}; for the last compound (un sym.) = 2.8×10^{-7}]. 713

b) In vitro choline esterase(s) inhibition is weak, but OMPA is converted in vivo (by liver) to a potent inhibitory substance—the conversion being enzymatic. 1837,745 493

(1) In vivo, the acute LD does not depress brain choline esterase, but more than 50% choline esterase depression occurs at sub-acute (100 ppm) feeding at which level erythrocyte and plasma choline esterase(s) inhibition occurs, with maximum attained in 4 hours after administration. 1057

(2) Schema: 497,3132

(a) OMPA $\xrightarrow[\left(\substack{\text{or oxidation with}\\ \text{neutral permanganate}}\right)]{\left(\substack{\text{Biological enzyme}\\ \text{action in vivo}}\right)}$ a substance (I) 1,000,000 times >effective than OMPA as inhibitor of choline esterase(s), chymotrypsin $\xrightarrow[\text{oxidation}]{\text{further}}$ a complex demethylation reaction.

(b) I = octamethyl pyrophosphoramide N-oxide (the most effective anticholinesterase metabolite).

(c) Chymotrypsin inhibiting action dependent on hydrolytic lability of compounds subsequently derived from I.

(d) Reaction (a) (oxidation at N of a dimethylphosphoramide group) converts a relatively stable pyrophosphoramide to a reactive phosphorylating agent, the monophosphoramide of OMPA.

(e) Interpretation:

Specificity vs. ChE conferred (?) by electron attracting N-oxide group; chromatography shows: (A) An unstable anti-ChE substance; (B) a more stable oxidation product. Chymotrypsin is phosphorylated in a mole for mole reaction, the enzyme combining with either phosphorus moiety of the oxidized pyrophosphoramide.

Initial step: Attack on one amide-N to give phosphoramide-N oxide; pyrophosphate linkage remains intact.

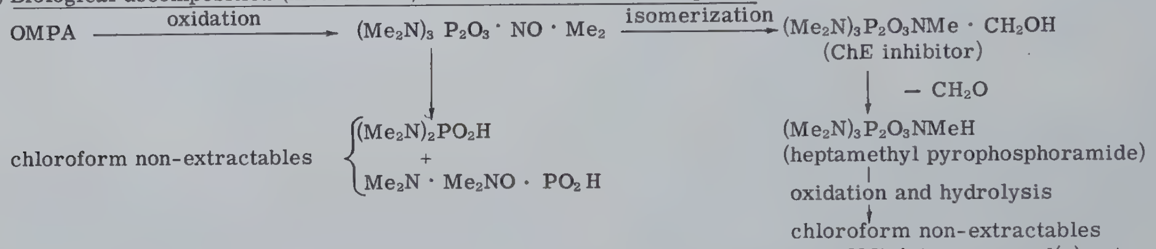
Oxidation of more than one dimethylamide to N-oxide yields a (?) compound unstable and at once hydrolyzed.

Highest anti-ChE activity is associated with initial step; other products are less active.

(f) Initial product of permanganate oxidation is same as the active biological derivative of OMPA, viz., monophosphoramide N-oxide of octamethyl pyrophosphoramide (liver metabolite).

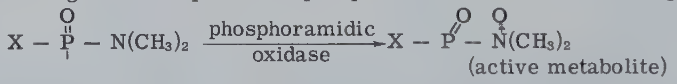
Compound	Partition Coefficient $CHCl_3/H_2O$	ID_{50}
Liver metabolite	1.42	$3.6 \times 10^{-7}M$
Permanganate oxidized OMPA	1.27	$4.0 \times 10^{-7}M$

(3) Biological decomposition (metabolism) of OMPA in animals and plants; schema: 1471


OMPA
oxidation
$(Me_2N)_3\ P_2O_3 \cdot NO \cdot Me_2$
isomerization
$(Me_2N)_3P_2O_3NMe \cdot CH_2OH$
(ChE inhibitor)
$- CH_2O$
chloroform non-extractables
$(Me_2N)_2PO_2H$
+
$Me_2N \cdot Me_2NO \cdot PO_2H$
$(Me_2N)_3P_2O_3NMeH$
(heptamethyl pyrophosphoramide)
oxidation and hydrolysis
chloroform non-extractables

(I) Aqueous H_2O_2, oxygenated liver slices and various plant species, convert OMPA to compound(s) not extractable from H_2O by CH_3Cl, to heptamethyl (HMPA) pyrophosphoramide and an inhibitor of ChE not separable by partition chromatography from HMPA. From all three sources, the ChE inhibiting substances appear to be the same.

(II) To effect the biological decomposition a phosphoramidic oxidase has been proposed: 497



$$X - \overset{O}{\overset{\|}{P}} - N(CH_3)_2 \xrightarrow[\text{oxidase}]{\text{phosphoramidic}} X - \overset{O}{\overset{/\!/}{P}} - \overset{O}{\overset{\uparrow}{N}}(CH_3)_2$$

(active metabolite)

c) Mode of action:

(1) OMPA is a cholinergic agent whose activity is developed in vivo by metabolic conversion. In consequence, 852
the onset of toxic symptoms is relatively delayed. Choline esterase of peripheral tissue is strongly 714
inhibited without marked inhibition of brain ChE. Hepatectomy (rat) decreases toxicity of OMPA. 237

(2) In consequence of the foregoing, the central nervous manifestations associated with poisoning by many 714
other organic phosphate insecticides are observed seldom with OMPA. 237

(3) Effects and symptoms are muscarinic from selective (relatively) parasympathetic stimulation (without 852
CNS effects) for which atropine is the effective antidote of at least 4 LD_{50} dosages (in contrast to 497
parathion and alkyl phosphates).

(4) Very toxic via the oral or cutaneous routes (280-560 mg = estimated dangerous dose [man]); myasthenia 497
gravis patients have received 25 mg per day for 3 weeks without toxic signs.

(a) LD_{50} (oral) of the symmetrical analogue (dimethylamido linkage with ethoxy group on each P atom) 852
= 11.5 mg/k (Rat); LD_{50} of unsymmetrical analogue (ethoxy and dimethyl amido groups on different
P atoms) = 2.7 mg/k, oral (Rat).

(b) Animals build a definite resistance on exposure to OMPA. ♀♀ are more resistant than ♂♂ (rats). 497

(c) A given amount of OMPA in vivo has 5000 times the ChE inhibitory action of the equivalent in vitro 497
(as tested in blood of rabbit treated with OMPA.) Activated in liver and in vitro by liver slices. 2651
Hepatectomy protects from otherwise toxic doses. Cumulative effect noted with repeated small
doses.

d) Symptoms of intoxication: Include: Anorexia, nausea, vomiting, abdominal cramp-like pain, excess 237
sweating and salivation; followed by pallor, miosis, diarrhoea, involuntary urination and defecation, lung
oedema, cyanosis.

(1) A complex of nicotinic effects may also appear which are not controllable by atropine.

e) Health hazards of the OMPA metabolite(s) in plants; Residues: 497

(1) No toxic effects in feeding tests. Decomposition products (chloroform non-extractables) produce no 2651
symptoms at levels in which the precursor is lethal.

(2) The monophosphoramide oxide (1st oxidation product) in oxidation mixtures where it is present to 5% is no more toxic (to rat) than OMPA per se.

(3) Stability of the metabolite depends on pH; half-life: Few hours to 2-3 days; OMPA half-life in plants: 2 weeks.

(4) Concluded that metabolite in plants is lost prior to absorption by the animal body, however the unconverted OMPA remaining in plant tissues is a hazard. A tolerance level of <3 ppm in plant tissue has been proposed.

(5) Residues in fruit of strawberries treated at 10 lbs per acre fell from 158.5 mg/k immediately after spraying to 5.6 mg/k in 30 days; at 1 lb per acre from 30.4 mg/k to 3.53 mg/k in 23 days. Minimum of 4 weeks should elapse between spray and pick. 1267

(6) OMPA (P^{32} labelled) sprayed at 1.0 lb per acre on cotton: After 41 days showed great affinity for oily seeds (8-16 ppm present in raw oil); on refining, content dropped to 0.02 ppm. Ground meal and cake contained 70-80 ppm of radioactive P^{32} (as OMPA), but H_2O/NaOH partition indicated complete metabolism to acid products. 2235

4) Phytotoxicity:

a) General: Not markedly phytotoxic at prescribed concentrations: more than 4 lbs per acre have proved injurious to some crops. 129 2120

b) Harmless (even at high concentrations) to: Brussels sprouts, sugar beets, hops; at moderate concentrations peas develop necrotic spots; at light concentrations (0.05% and over) broad beans (*Vicia faba*) develop necrotic areas in 3 weeks. Potatoes: Susceptible to injury under some conditions; defoliation and fruit drop noted in some apple varieties. 2655

c) Not sufficiently innocuous for hydroponic use with plants. 216

d) May accelerate or inhibit plant growth; at high concentration on peas gave an initial decline in growth rate, followed by spot and marginal chlorosis then necrosis; as a soil application, injury appears first on lower leaves; only in extreme cases is there injury of terminal growth. 494

(1) At 1000 ppm of OMPA *per se* [as the tech. grade (42% OMPA)] significantly more phytotoxic than a purified sample (70% OMPA).

(2) No phytotoxicity (peas) at 200 ppm.

(3) Low concentrations may accelerate growth (peas).

e) As in animals, phytotoxicity is attributed to the metabolite (monophosphoramide oxide of OMPA); a direct relationship was noted between the amount of OMPA in the plant, the inactivation of plant phosphatase enzymes and phytotoxicity; the metabolite inhibits phosphatase and essential plant enzymes. 497

(1) Identity of plant and animal metabolite was established by chromatography.

(2) Induced chemical changes in plant resembling the action of 2,4-D: Increase in carbohydrate and nitrate in the composition of beans, peas; effects more pronounced in sun-illuminated plants than in plants in darkness. 672

f) Phytotoxic to corn in soil treated at 1257 mg per plant. 3181

5) Systemic activity in plants:

a) As a systemic insecticide in aerosols, water and foliage sprays, OMPA is reported to destroy by systemic action (there being no contact action) both the non-resistant and resistant "populations" of 2-spotted spider mite in the active stages. Non-R biotypes were killed in 1-2 days earlier than R biotypes. The action is said to be wholly systemic via the plant juices and the acaricidal property is retained 2 to 4 weeks or more by treated plants. 2867

b) OMPA is rapidly absorbed and translocated after application to plants by various routes, such as application to foliage, to roots via soil or water, roots in water cultures, as a seed-soak, via bark or stems. 2651,201 219,3181 3220,3081

(1) The effectiveness of the route of application depends on many factors in the nature of the plant, age of foliage, environment, etc. 2876,1417 2246,672

(2) Sprayed for example on leaves of apple, beans, *Coleus*, *Chrysanthemum*: Some is absorbed, some evaporated, some remains as a leachable residue. 1267,1695 3257,1130

(3) Temperature, illumination, age of foliage and species affect the absorption. 694

(4) Rate of plant growth influences the persistence of OMPA in the plant.

(5) Light is of great importance in translocation (which is mainly upward) although there is also downward movement, particularly if foliage is treated.

(6) Movement may be mainly in the phloem (as in apple tree) but may be in the xylem (especially in upward movement).

(7) OMPA (or the metabolites) must attain a concentration in the tissues and juices which is insecticidal or acaricidal.

(8) Stage in the plant's life-cycle is a factor, thus translocation is minimal in bean plants in bloom, as compared with young plants in the 6, 8, or 10-leaf stage. Young leaves of apple are more absorptive than older leaves.

(9) In corn and bean plants, ca. 40% of the applied OMPA or its active derivative was present in the *untreated* leaves of the plants 12 days after application to treated leaves; OMPA exceeded para-oxon and parathion in translocation capacity, in that order; the toxic effect persisted longer than 4 weeks and surpassed para-oxon and parathion.

(10) Solubility of OMPA in water is of prime importance in systemic capacity, thus OMPA is water miscible, para-oxon is soluble to 0.24%, parathion to 0.0024% and systemic action is directly related to these solubilities.

(11) OMPA passes preferentially into young growing parts of such plants as beans, cabbage, hops, peas and strawberries and concentrates in the most rapidly growing leaf parts. Up to 10% of the OMPA applied to one bean leaf is translocated to the *untreated* leaves. Translocation to terminal leaves is stronger on bark application, to median leaves via root application. In bean, absorption is slower in soil than in sand culture.

(12) By soil treatment, injection into trunk or application to bark, OMPA may pass (in insecticidal concentration) to all parts of even tall trees.

c) Treatment of a single leaf (or a few leaves) results in much more limited movement, for instance 15 cm down and 17 cm up in Chrysanthemum; sprayed on leaves of flowering cabbage, OMPA moved up 3 feet to flower buds; on citrus acaricidal amounts appeared 16 inches down and 19 inches up from treated leaves; translocated via stolons from parent to daughter strawberry plants. 2651

d) Vs. certain root aphids, such as those of lettuce or primroses OMPA has given outstanding success by being "watered" on the soil. 2651

e) OMPA was readily absorbed and transported from roots of lemon tree seedlings to leaves in increasing amounts over 46 days; leaf juices became appreciably toxic for Paratetranychus citri in 12 to 24 hours. Translocation was greatest in the direction of the most rapidly growing leaves. Applied to bark of orange seedlings, OMPA was quickly translocated to leaves (notably terminal leaves) in amounts highly toxic to P. citri. Absorption via bark is more effective than from roots in water culture. 2246

(1) Absorbed from lemon leaves: 50% of the applied OMPA inside plant in 48 hrs; treatment of one leaf: 0.1%-1% of total dosage in other leaves in 17 days.

(2) Applied to lemon and orange fruits peel absorption is rapid, but penetration to pulp low: 0.03 ppm in juice from application of 0.036% H_2O solution after 18 days; 0.42 ppm from 0.1% solution after 42 days.

(3) Concentrations of 20 to 50 µg/g leaf tissue were lethal, in 48 hrs, to adult ♀ Paratetranychus citri; 4000 µg/g leaf were required to kill adult ♀ Heliothrips haemorrhoidalis.

f) Leaf juices from OMPA containing lemon plants proved but slightly effective as Musca brain ChE inhibitors; activity was largely independent of total OMPA concentration; it was postulated that the toxic metabolite formed is quickly broken down and does not accumulate as do OMPA proper and the inactive metabolites. 2246

g) Fate of OMPA in plants:

(1) Breakdown into chloroform non-extractable substances varies with species, being greatly more for example in beans than in Coleus; breakdown is similar in all plant parts (Chrysanthemum, apple, beans, Coleus), but may be (?) higher in untreated portions of plant. 50% was decomposed in Vicia faba in 8 days. 201,219 3081,694

(2) Phytotoxic effects are ascribed to the same active metabolite formed by metabolism of OMPA in mammals (the monophosphoramide oxide of OMPA) which inhibits phosphatase and essential plant enzymes. The essential similarity of metabolic breakdown and the products of breakdown in animals, plants and chemical oxidation appears well substantiated. (See preceding treatment of the fate of OMPA in higher animals.) 1471 497

(3) Comparative toxicity to Aëdes aegypti larvae of OMPA and para-oxon (the pure substances, extracts of treated leaves and leaves adjacent to treated leaves of Vicia faba): 672

Compound	Pure Substance Only LC_{50} (ppm)	Pure Substance Only LC_{90} (ppm)	Extract Of Treated Leaves LC_{90} (ppm)	Extract Of Untreated Adjacent Or Lower Leaves LC_{90} (ppm)	Estimated % Of Applied Toxicant Recovered
OMPA	0.29	0.95	1.05	12.5	7.6-8.0
Para-oxon	0.007	0.016	0.017	0.75	2-2.2

(4) In the case of aphids, OMPA itself is considered the substance which is received systemically from the treated host plant and which is then in the insect converted to the active ChE-inhibiting toxic metabolite. 2651

(5) The plant metabolite is said to be (probably) more important as a toxic agent for insects than for mammals, because of less drastic pH changes involved in ingestion and absorption by the insect body, since the stability of the metabolite depends on pH and has a half-life of from a few hours to 2-3 days. 497

h) Tests of systemic action of OMPA in plants:

(1) Mortality of Tetranychus bimaculatus in 5 day exposures to bean plants previously treated by 3 day exposures (roots) to solutions of 5 to 10 ppm concentration; laboratory tests: 3220

[A] Via Roots; In Solution

µg OMPA/g plant	% Kill (corrected)
7.2	38
7.8	42
8.2	49
9.7	52
12.3	70
12.4	77
14.0	76
15.0	87
16.0	90
18.0	90
20.0	98
22.5	99
24.0	94

[B] OMPA Deposit On Dipped Bean Leaves And % Mortality Of T. bimaculatus

% Concentration of OMPA	µg/gram plant	% Kill (corrected)
0.02	47 (39-54)	86.6(82-93)
.014	28 (26-31)	78.3(68-86)
.01	20.2(16-24.5)	70 (59-76)

LD_{95} calculated as 82µg OMPA deposit/gram plant.

[C] Mites Exposed 7 Days On Bean Plants Watered With 100cc Of OMPA Solutions In 500cc Pots:

% Concentration OMPA	Sand Culture % Kill	Soil Culture % Kill
0.1	96	99
0.05	90	85
0.025	52	50

[D] *T. bimaculatus* exposed for 5 days to bean plants cut from roots 3 days after treatment with OMPA via roots:

% Concentration OMPA	% Kill In	
	Sand Culture*	Soil Culture
0.1	100	97
0.05	100	87.5
0.025	100	74

*Root systems more extensive in sand culture.
LD_{95} calculated as 6500 μg OMPA/gram of cut plant.

(2) OMPA* and Isopestox® vs. *Tetranychus telarius* on *Hydrangea*: 1267

Insecticide (Systemic)	Method	Concentration (%)	% Mortality
OMPA	Soil watering	0.1%	56
Isopestox®	" "	.05%	99
OMPA	Foliage spray	0.1%	75.5
Isopestox®	" "	.05%	98.5

*The effect of OMPA on mites, as interpreted from this experience, is stated to be by contact mainly and not by systemic action. Vs. *Myzus persicae* and *Macrosiphum gei* OMPA gave complete control on tulips, either as a 0.3% spray or as 100cc of 0.3% solution applied by watering to 500 grams soil.

(3) Effectiveness of OMPA, by systemic action in soil applications to potted plants, vs. the associated pests; applied in water (1:600) solution, comparable on basis of soil volume of pots of various sizes: 2876

cc/Pot	Plant	Pests Present	Effect On Pest*	Plant Injury
7.5	Bean	*Tetranychus bimaculatus*	Death in 6 days.	0
15	"	" "	" "	0
30	"	" "	" "	Moderate
30	"	*Epilachna varivestis*	0	"
22.5	*Chrysanthemum*	*Anuraphis helichrysi*	Death in 4 days.	0
22.5	"	*Aphis gossypii*	" "	0
22.5	"	*Rhopalosiphum rufomaculatum*	" "	0
22.6	"	*Hercinothrips femoralis*	0	0
22.5	"	*Phenococcus gossypii*	0	0
22.5	"	*Trialeurodes vaporariorum*	0	0
90.0	"	same pests as above	Same effect as above.	Slight
180.0	"			Moderate
22.5	*Lilium longiflorum*	*Aphis gossypii*	Death in 4 days.	0
90	" "	" "	" "	0
180	" "	" "	" "	0
22.5	Potato	*Aphis gossypii*	Death in 6 days.	0
22.5	"	*Myzus convolvuli*	" "	0
22.5	"	*Macrosiphum solanifolii*	" "	0
22.5	"	Hemitarsonemus latus	0	0
22.5	"	*Trialeurodes vaporariorum*	0	0
90	"	Same pests as above	Same effect as above.	Slight
180	"			Severe
22.5	*Rosa*	*Tetranychus bimaculatus*	Death in 10 days.	0
7.5	*Saint Paulia*	*Tarsonemus pallidus*	0	0
30	" "	" "	0	0
60	" "	" "	0	0
18	Turnip	*Myzus persicae*	Death in 4 days.	0
36	"	" "	" "	0
36	"	" "	88% kill after 20 days from plant treatment.	0
76	"	" "	99% "	0

*N.B. A general high effectiveness for aphids; ineffectiveness vs. thrips, white fly and mites.

(4) Practical: At 0.6 lb per acre (0.6k per hectare), followed by 1.3 lb per acre when plants were at full height, controlled *Phorodon humuli* on hops; age of foliage affects systemic uptake; foliage application: Vs. *Pentatrichopus fragaefolii* on strawberry control was given by 1 lb per acre in mid-May repeated in June on non-fruiting plants. Only one spraying at the end of April is permissible for fruiting plants. Persistence is affected by rate of plant growth, the toxic effect on insects enduring 2 to 3 weeks in July to more than 15 weeks in November-treated plants. 0.75 lb per acre controlled *P. fragaefolii*, but to control *Amphorophora rubi*, *Macrosiphum rosae* and *Macrosiphum euphorbiae* 7 lbs per acre constituted the lowest dosage for control. 1267 1687

(5) Toxic Threshold Concentrations of OMPA in plant tissue vs. certain aphids and other arthropods: 201,219 3081,2231

Insect Or Arthropod	Toxic Threshold Concentration (µg/gram Of Fresh Wgt Tissue)
Aphis fabae	10-15 (20-25 ppm)
Macrosiphoniella sanborni	20-25
Aphis pomi	20-30
Paratetranychus citri	20-25 ppm
Heliothrips haemorrhoidalis	4000 ppm

(6) Entrance of OMPA into plants; quantitative experiments: 2231

Leaves Dipped In 0.1% Solutions		
Time (After Exposure) (Hours)	% In Leaf Interior: Bean	% In Leaf Interior: Lemon
1	7	6.8
5-6	38	18
24	69.5	43.9
72	80.5	76.5

20 Microliters (0.1% Solution) Applied To Stem (Lemon Plants)		
Time(After Exposure) (Days)	**PPM In Upper Leaves	Partition: HCCl$_3$/N NaOH*
1	153	21.7
2	375	13.8
4-5	546	15.6
14	888	11.3
28	1515	7.1

*Constitutes a measure of breakdown of OMPA in plant tissues, since the ultimate metabolites are chloroform insoluble; partition coefficient OMPA chloroform/N NaOH = 24.1.

**% found in various parts of plants: Basal 12.7%; median 22.3%; terminal 65%.

(a) Applied to broad beans (Vicia faba) via roots from 0.05% solutions: 163 µg/gram leaf appeared in plant interior in 3 days.

(b) Lemons, growing in 0.0059% solutions: 309 ppm appeared in leaf tissue after 4 weeks; in 0.036% solutions 4500 ppm appeared in leaf tissue after 46 days; in bean 38% of total OMPA in the plant was in leaves after 7 days; in lemon after 47 days 69% of total OMPA in plant was in the leaves.

(c) Required to make Vicia faba toxic to Aphis fabae on the leaves by root application are solutions of 0.005% strength; in case of para-oxon the concentration must be 0.04%.

(d) The systemic residues in plants disappear over several weeks to several months, the disappearance being more rapid in periods of high plant metabolism, such as Spring season. The rate of disappearance is, however, independent of plant species. The disappearance is by enzymatic metabolism and not by volatilization loss.

6) Toxicity for insects:

a) By contact OMPA is non-toxic for some insects yet highly toxic for others. 353

b) Quantitative

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti (larva)	Medium	LC$_{50}$	0.29 ppm	Para-oxon LC$_{50}$ = 0.007 ppm.	672
Aëdes aegypti (")	Medium	LC$_{90}$	0.95 ppm	" LC$_{90}$ = 0.016 ppm.	672
Aëdes aegypti (3rd instar larva)	Medium	LC$_{50}$ 72 hr	0.3 ppm		2507
Aëdes aegypti (")	Medium	LC$_{90}$ 72 hr	1.0 ppm		2507
Aphis medicaginis (1st instar nymph)	Contact Spray	LC$_{100}$ 20 hr	0.05% w/v	0.005% w/v gave 10% kill in 20 hr, 0.5% w/v = 100% kill in 20 hr.	2507
Aphis medicaginis (")	or	LC$_{50}$ 24 hr	270 µg/gram leaf	Feeding on OMPA infiltrated bean leaves.	2507
Aphis fabae	or	Toxic Threshold	10-15 µg/g (leaf fresh wgt)	Feeding on systemically treated plants.	201,219,3081
Aphis pomi	or	Toxic Threshold	20-30 µg/g "	" "	201,219,3081
Anasa tristis	inj	LD$_{50}$	16 µg/g	Considered an OMPA susceptible insect.	2392
Anasa tristis	Topical	LD$_{50}$	16 µg/g	Metcalf quoting Ref. 2392.	2231
Apis mellifera (adult)	or	LD$_{100}$ 24 hr	25 mg x 10^{-2}/bee		1719
Apis mellifera (")	or	LD$_{50}$ 24 hr	ca10-15 mg x 10^{-2}/bee		1719
Apis mellifera (")	or	LD$_{10}$ 24 hr	ca5 mg x 10^{-2}/bee		1719
Apis mellifera (")	Residue Contact	LDeposit$_{35}$ 24 hr	ca65 mg x 10^{-3}/cm^2		1719
Apis mellifera (")	Topical	LD$_{50}$	> 100 µg/g	Considered OMPA "non-susceptible" insect.	2392
Culex quinquefasciatus (larva)	Medium	LC$_{50}$ 48 hr	35 ppm		2507
C. quinquefasciatus (larva)	Medium	LC$_{90}$ 48 hr	62 ppm		2507
C. quinquefasciatus (3, 4th instar)	Medium	LC$_{50}$ 48 hr	49 ppm	As tech. OMPA.	2507
C. quinquefasciatus (")	Medium	LC$_{90}$ 48 hr	80 ppm	" "	2507
C. quinquefasciatus (")	Medium	LC$_{50}$ 48 hr	35 ppm	As pure OMPA.	2507
C. quinquefasciatus (")	Medium	LC$_{90}$ 48 hr	60 ppm	" "	2507
C. quinquefasciatus (")	Medium	LC$_{50}$ 48 hr	29 ppm	P^{32} labelled OMPA.	2507
C. quinquefasciatus (")	Medium	LC$_{90}$ 48 hr	50 ppm	P^{32} " "	2507
Cytorhinus mundulus	Contact Spray	LC$_{50}$ 24 hr	1.773 mg/cc (1.58-1.99)	Spray tower application.	3181
Aphis fabae	or (Systemic)	MLC	0.005%	As solution to roots of bean host. BFPO = 0.002%, Na fluoroacetate = .0002%, nicotine = .01%.	695 702 7031
Heliothrips haemorrhoidalis	or (Systemic)	MLC	4000 µg/g fresh citrus leaf	Feeding on systemically treated plant.	2507
Macrosiphoniella sanborni	or (Systemic)	MLC	20-25 µg/g fresh wgt plant tissue	" "	201,219,3081
Musca domestica (adult)	Topical	LD$_{50}$	> 500 µg/g	Considered an OMPA "non-susceptible" insect.	2392

b) Quantitative

Insect	Route	Dose	Dosage	Remarks	
Metatetranychus citri (adult ♀)	or	LC_{50} 24 hr	88 ppm	Experimental feeding, water solution; directly active.	2507
Metatetranychus citri (")	or	LC_{50} 48 hr	36 ppm	" " "	2507
Metatetranychus citri (")	or	LC_{90} 48 hr	80 ppm	" " "	2507
Lachnus saligenus	Topical	LD_{50}	22 μg/g	Considered OMPA "susceptible" insect.	2392,878
Leptinotarsa decemlineata	inj	LD_{50}	"massive"	" "non-susceptible" insect.	2392
Oncopeltus fasciatus	Topical, inj	LD_{50}	ca30 μg/g	" "susceptible" insect.	2392,2231
Phormia regina (adult)	inj	LD_{50}	175 μg/g	" "non-susceptible" insect	2392
Periplaneta americana (adult)	Topical	LD_{50}	> 100 μg/g	" "	2392,2244
Periplaneta americana (")	inj	LD_{50}	> 100 μg/g	" "	2244
Peregrinus maidis	Contact Spray	LC_{50} 24 hr	0.58 (0.569-0.592)mg/cc	Spray tower application.	3181
Pyrrhocoris apterus	Topical	LD_{50}	34 μg/g	Considered an OMPA "susceptible" insect.	878,2392
Tenebrio molitor (larva)	inj	LD_{50}	> 100 μg/g	Considered "non-susceptible".	2392,2244
Tetranychus bimaculatus		LD_{95}	82 μg deposit/g wgt plant	Dipped foliage.	3220
Tetranychus bimaculatus	Systemic	LD_{95}	6500 μg/g treated plant		3220
Vanessa antiopa (larva)	inj	LD_{50}	> 400 μg/g	Considered "non-susceptible".	2392
Tetranychus bimaculatus	Systemic	LC_{95}	20 mg/k plant (bean)	OMPA taken up via cut stem.	2651,3220
Tetranychus bimaculatus	Systemic	LC_{95}	82 mg/k plant (bean)	" from spray deposit.	2651,3220
Aphis fabae	Systemic	LC_{100}	50 mg/k plant (bean)	As unaltered OMPA in plant.	694

b) Comparative toxicity, OMPA, others:

(1) Vs. certain aphids: 18

Insecticide	Insect	Conc %	% Mortality After			
			24 hrs.	72 hrs.	120 hrs.	456 hrs.
OMPA	Aphis pomi	0.06	73.9	91	97.7	100
Pyrazothion	" "	0.02	98.2	99.7	99.4	100
Diazinon	" "	0.02	85.7	90.9	73	30
Pyrazoxon	" "	0.02	96.5	100	98.5	96
OMPA	Sappaphis plantaginea	0.06	—	—	—	—
Pyrazothion	" "	0.02	5	100	100	100
Diazinon	" "	0.02	94.8	100	100	100
Pyrazoxon	" "	0.02	99.3	100	100	100

(2) Systemic action vs. Tetranychus bimaculatus via bean plants dipped (roots) in insecticides in Knop's Solution; 1121

M = mobile stage
R = resting stage :
E = eggs

Insecticide	Conc. g/100 liters	Mite "Population" At								
		Start			4 days later			6 days later		
		M	R	E	M	R	E	M	R	E
OMPA	10	11	8	45	0	0	38	2	0	31
"	20	14	4	31	0	0	31	0	0	27
Pyrazothion	10	21	6	24	14	1	36	16	0	40
"	20	19	11	14	15	0	15	8	0	26
Pyrazoxon	10	12	5	49	0	0	14	0	0	2
"	20	14	8	22	0	0	8	0	0	1
Diazinon	10	18	12	19	9	4	23	13	0	30
"	20	17	24	9	4	8	28	9	0	29
Systox®	10	20	0	12	0	0	12	0	0	6
"	20	14	4	34	0	0	34	0	0	26
Control		27	13	18	48	26	121	156	29	203

(3) Vs. Phaedon cochleariae, by direct contact and systemic application: 704

Insecticide	Required To Give 100% Mortality					
	By Dipping (% Concentration)			Systemic from soil (cc/$3\frac{1}{2}$ in. pot with 400g compost)		
	Aphis	Pieris	Phaedon	Aphis	Pieris	Phaedon
OMPA	.05	>.2	>1.0	.02	>.04	>.1
Dimefox	.05	>.1	> .5	.002	>.02	.01
Sodium fluoroacetate	.001	>.1	> .1	.001	.02	>.1
Para-oxon	.0005	.01	.01	>.04g	.002g	.002g

(a) OMPA is ineffective systemically vs. Phaedon cochleariae.

(b) By direct contact, OMPA is less effective vs. Phaedon than para-oxon, sodium fluoroacetate or dimefox. Adults are more resistant than larvae.

(4) Time (in hours) required for 100% mortality of Tetranychus bimaculatus on leaves of maize (Zea mays) or broad bean (Vicia faba) immersed at petiole (bean) cut end of leaf (maize); temperature range: Maize 62-86°F; bean 60°-90°F: 672

Compound	% Conc.	Time (Hrs) For 100% Kills On Maize Leaves	 Bean Leaves
OMPA	0.005	48 ± 2	48 ± 5
"	.02	45 ± 2	30 ± 3
"	.05	40 ± 3	24 ± 2
Para-oxon	.005	120 ± 6	48 ± 5
"	.02	72 ± 5	18 ± 2
"	.05	48 ± 5	12 ± 3
Parathion	.005	< 100% kill in 96 hrs	60 ± 4
"	.02	< " "	40 ± 2
"	.05	120 ± 8	30 ± 3

(a) Fumigant Effect, OMPA and others vs. Tetranychus bimaculatus, on the leaves of untreated Vicia faba, enclosed at 60°-80°F beneath a bell jar with a treated plant; 300 mites per test with 3 replicates:

Compound	% Conc.	1 Week Mortality (Corrected) (%)
OMPA	0.05	3.5 ± 2*
"	.02	0*
Parathion	.05	68 ± 8**
"	.02	29 ± 5
Para-oxon	.05	29 ± 5
"	.02	12 ± 4

*Little, if any, fumigant action. **Marked fumigant action.

c) Toxicity for beneficial insects:

(1) Vs. Apis mellifera, with observations on possible contamination of honey via OMPA - containing flower nectars: 1719

(a) Toxicity for Apis (as a stomach and contact poison) is considered low.

Oral Administration Dose/Bee (mg x 10^{-2})	 % Kill 24 hrs	Contact Spray Dose/Bee (mg/cm^2 x 10^{-3})	 % Kill 24 hrs	Dry Film Residues Dose/Bee (mg/cm^2 x 10^{-3})	 % Kill 24 Hrs
25	100	65	35	0.06	7
20	85	31	25	—	—
15	64	6.5	22	—	—
10	47	3.1	0	—	—
8	17	—	—	—	—
5	10	—	—	—	—
Parathion (mg x 10^{-5})		Parathion		Parathion	
70	100	64	100	0.06	100
25	85	51	82.5		
6	60	42	70.0		
3	43	36	42.5		
2.5	28	35	20.0		
.5	0	5	0		

Spray applications of OMPA to mustard and borage (using P^{32} labelled insecticide) revealed contamination of nectar. There is no breakdown of OMPA in the bee's honey stomach; OMPA remains stable for > 2.5 months in contact with honey. OMPA may appear in unchanged form in honey derived from the nectar of plants sprayed more than 4 weeks before bee foraging on the treated plants. 1719

(2) Vs. Cyrtorhinus mundulus, an egg-predator of Peregrinus maidis (corn leafhopper):

(a) Contact toxicity, LC_{50} 24 Hrs By Spray tower Application:

	OMPA	Systox®
P. maidis	0.58 (.569-.592) mg/cc	0.044 (.041-.046) mg/cc
C. mundulus	1.773 (1.578-1.99) mg/cc	0.037 (.031-.044) mg/cc

(b) Mortality of pest and predator on corn plants treated systemically (via the roots) with OMPA and Systox® :

Insecticide	mg/plant	% Mortality On Various Days After Treatment C. mundulus 1 day	 7 days	 P. maidis 2 days	 7 days	 14 days	 21 days	 26 days	 40 days
OMPA	1257	10	0	100	100	100	93	84	Plant Dead
	943	5	10	100	100	100	93	86	95

(b) Mortality of pest and predator on corn plants treated systemically (via the roots) with OMPA and Systox® :

Insecticide	mg/plant	% Mortality On Various Days After Treatment C. mundulus 1 day	 7 days	 P. maidis 2 days	 7 days	 14 days	 21 days	 26 days	 40 days
OMPA	628	0	—	100	100	100	94	76	89
	314	0	—	95	100	92	73	83	80
	63	0	—	47	88	90	58	77	47
Systox®	500	—	—	100	100	100	100	Plant Dead	
	50	—	—	100	100	100	96	86	47
	25	100	10	100	100	89	75	73	13
	12.5	80	25	100	100	67	47	5	—
	5.0	20	0	100	91	33	25	0	—
	2.5	20	10	—	—	—	—	—	—
	1.3	0	0	—	—	—	—	—	—
	.5	—	—	14	5	0	0	0	—

OMPA is ca. 3 times as toxic to the pest insect P. maidis as to the useful predator C. mundulus, whereas Systox® is equally toxic to pest and predator.

(3) Mortality of Brevicoryne brassicae and its insect enemies on cabbage plants sprayed with OMPA at 2 cc per plant; concentration 0.4%: 2651

Insect	% Mortality After 24 hrs	 10 days	 20 days	 30 days	 40 days
Brevicoryne brassicae (cabbage aphid)	95	86	83	22	8
Coccinella septempunctata	0	2	0	0	0
Syrpha (larvae)	0	0	0	0	0
Aphidius brassicae	25	0	0	0	0

Exposed on plants after treatment with OMPA via the soil; OMPA concentration 0.4%.

Dosage (cc/plant)	Insect	% Mortality After 24 hrs	 10 days	 20 days	 30 days	 40 days
2	Brevicoryne brassicae	52	69	18	0	0
5	" "	82	53	45	30	16
10	" "	96	82	78	60	14
10	Aphidius brassicae	0	0	2	0	0
10	Coccinella septempunctata	0	0	0	0	0
10	Syrpha sp. (larva)	0	0	0	0	0

High selective action vs. pest; low toxic action vs. predators.

d) Pharmacological, pharmacodynamic, physiological, etc.; insects: (Also consult the corresponding treatment for higher animals).

(1) OMPA in vitro is a weak inhibitor of insect choline esterase(s), being inactive at 1 x 10^{-3} M for choline esterases of Apis mellifera, Periplaneta americana, Anasa tristis and Musca domestica. 2244 2392

(2) OMPA is non-toxic by contact for some insects but highly toxic for others. 2231

(3) To account for the fore-mentioned selectivity three suggestions have been made: I) the choline esterase(s) of susceptible species is particularly sensitive; II) the mode of feeding influences the possibility of high intake; III) only susceptible forms have enzyme systems to convert OMPA to an active toxic metabolite (ChE inhibitor). 2392 1616

(a) Insect tissues from both susceptible and non-susceptible species) convert OMPA to active anti-ChE.

(b) Differences between susceptibles and non-susceptibles is quantitative.

(c) Suggestion is made that only such OMPA as is converted in the nerve cord to active metabolite(s) takes part in poisoning. For example, in non-susceptibles so much OMPA is converted in the fat body that little reaches the nerve cord. Also suggested is a membrane barrier in the nerve cord to OMPA converted in other tissues to active metabolite (in mammals the peripheral effect is strong, CNS effect weak).

(4) OMPA poisoning develops relatively slowly and the toxic intermediate appears unstable.

(5) Conversion of OMPA in insects (as in plants and higher animals) is by a tissue enzyme system which may be inhibited in vitro by: Iodoacetic acid, hydroxylamine, sodium fluoride, mercuric chloride, sodium azide, malonic acid, cysteine, homogenization, heat, freezing, anaerobiosis.

(a) Various tissues of insects differ in their capacity to perform the conversion, thus in Periplaneta tissue capacity to convert OMPA decreases in the following order: fat body, hindgut, foregut, cuticle, nerve cord, (muscle is inactive); similar results in other insects. In two very susceptible forms (Anasa, Oncopeltus) the ability of the midgut to convert OMPA exceeds that of fat body.

(6) Topical application to OMPA-sensitives brings virtually complete brain ChE inhibition. 878

(7) Injection into Periplaneta of OMPA metabolite at 100 μg/g did not poison the insect although the in vitro product of OMPA conversion by Periplaneta gut is apparently identical with the active monophosphoramide oxide of OMPA identified from mammalian tissue and plant tissue conversion and in permanganate oxidation. 497 2393

(8) For certain OMPA non-susceptible insects (Trialeurodes vaporariorum; Blattella) doses 6 to 24 times larger than for Musca domestica were required of the active OMPA metabolite (from liver slice conversion) to inhibit ChE.

(9) Various schemata for OMPA biological conversion appear in the corresponding section for higher animals.

(10) Absorption of P^{32} labelled OMPA by larvae of Culex quinquefasciatus and metabolic fate (measured by partition between chloroform and normal sodium hydroxide) as measured at various intervals after administration (by contact) with OMPA in the medium at 60 ppm:

Contact With OMPA (60 ppm) (Hrs)	*Absorption And Metabolites (μg/g) In					
	Live Larvae			Dead Larvae		
	Total	In $CHCl_3$	In N NaOH	Total	In $CHCl_3$	In N NaOH
0.5	.005	0	.002	—	—	—
1.5	.009	.001	.008	—	—	—
3	.048	0	.034	—	—	—
7	.057	.003	.046	.020	.002	.007
12	.095	0	.038	.062	0	.032
24	.152	.003	.145	.104	.010	.086

*OMPA is metabolized (almost as rapidly as it is absorbed) to substances partitioning in favor of N NaOH. Living and dead larvae contained amounts of OMPA proportional to the concentration of the test solution and to the resulting mortality.

P^{32} OMPA In Medium (ppm)	% Mortality		*Absorption P^{32} OMPA And Metabolites In	
			Live larvae (μg/mg)	Dead larvae (μg/mg)
60	45	At 22 hrs	0.13	0.12
80	82	" 22 "	.2	.19
20	28	" 44 "	.07	.06
30	58	" 44 "	.09	.08
40	80	" 44 "	.12	.11

*Compared to larvae (which feed) pupae (non-feeding) which absorb OMPA via the cuticula, show only a small intake which is rapidly metabolized. The principal mode of entry into this insect, at least, is probably by ingestion.

(a) OMPA is appreciably toxic by direct contact to Aphis medicaginis (1st instar nymphs) treated by direct spraying:

Concentration % w/v	% Mortality (20 Hrs)
0.005	10
.05	100
.5	100
H_2O Control	0

and by the systemic route, i.e. feeding on leaves of bean plants containing translocated OMPA (stem application over 2 to 4 days before start of feeding tests).

P^{32} OMPA Conc. μg/g bean leaf	% Mortality (Aphis medicaginis)
180	53 in 48 hrs
320	65 in 48 hrs
420	75 "
530	80 "
630	86 "
760	88 "

(b) On bean leaves infiltrated with OMPA (270 μg/g leaf), 50% kills at 24 hrs, and 60% kills at 60 hrs were registered; at intervals of: Immediately, 24, 48, 72 hrs after infiltration, no real differences in toxicity of leaves appeared except in presence of high evaporation or detoxification.

(c) LD_{50} and LD_{90} values in these experiments for Metatetranychus citri (direct experimental feeding) Culex quinquefasciatus (larvae) and Aëdes aegypti (3rd instar larvae) (application via medium with ingestion presumed):

Insect	LC_{50}	LC_{90}
Metatetranychus citri*	88 ppm (24 hr LC_{50})	—
" "	36 ppm (48 hr LC_{50})	80 ppm (48 hr LC_{90})
Culex quinquefasciatus (3, 4th instar)	35 ppm (")	62 ppm (")
" (")	49 ppm (")	80 ppm (") tech. OMPA.
" (")	35 ppm (")	60 ppm (") pure OMPA.
" (")	29 ppm (")	50 ppm (") P^{32} labelled OMPA.

*Fed upon "liver-activated" OMPA (OMPA incubated with mouse liver slices for 0.5, 1, 2 hours) the toxicity proved not markedly different.

(d) In case of Culex, Metatetranychus and Aphis no real difference in toxicity was revealed for comparable amounts of OMPA and of OMPA after exposure to plant or animal tissues. The unchanged OMPA is metabolized in insects to compounds which include an active metabolite responsible for the toxic effect; the small amount of the active metabolite which is produced in plant tissues, when ingested with considerably larger quantities of unchanged OMPA received via the "systemic" route, is of little import in relation to the toxicity of OMPA per se by this application method.

(e) For Aphis fabae the concentration of undecomposed OMPA necessary for 100% kill via the systemic route on beans = 50 mg per k plant tissue; mortality of Aphis began at 20 mg per k plant tissue. 20-50 mg per k citrus leaf were required for 50% kills of citrus red-mite in 48 hrs, 50-100 mg per k for 100% kills in 24 hours; for 100% kills of Heliothrips haemorrhoidalis 4000 mg per k leaf tissue were needed. Dead aphids (from plants systemically treated and yielding 50% kills of Aphis) contained 15-20 mg OMPA anhydride per k. 694 2651

(f) Stimulates cytochrome oxidase of cockroach coxal muscle preparations in Warburg's apparatus. 2305

c) Field experiences in the control of economic insects with OMPA: 2651

Plant	Insect	Type Of Experience	Concentration (%)	Type Of Application	Result	Country
Apple, pear, plum	Anuraphis helichrysi	Field	0.04	Foliage Spray	99% kill	Switzerland
Apple	Anuraphis crataegi	"	.15	"	95% "	U.K. (=United Kingdom)
"	Tetranychus sp.	"	.05	"	100% "	Italy
"	Eriosoma lanigerum	"	.1	"	100% "	U.K.
"	Aspidiotus perniciosus	"	.05	"	45.6% kill	Italy
Cherry	Myzus cerasi	"	.067	"	93% kill	U.S.
Citrus	Paratetranychus citri	"	.1	"	100% "	U.S.
Sitka spruce	Neomyzaphis abietina	"	2.5	Soil	97% "	U.K.
Raspberry	Amphorophora rubi	"	.2	Foliage Spray	100% "	U.K.
"	Aphis ideae	"	.2	"	100% "	U.K.
Strawberry	Tarsonemus pallidus	"	.4	"	poor control	U.S.
"	Pentatrichopus fragaefolii	Greenhouse	.094	"	100% "	U.K.
Black currant	Tetranychus telarius	Field	.1	"	good control	U.K.
"	Dasyneura tetensis	"	.1	"	"	U.K.
Grape	Tetranychus sp.	"	.05	"	"	Italy
"	Eriophyes vitae	"	.05	"	"	Italy
"	Phylloxera (root)	"	.05	Soil	poor control	Germany
Potato	Aphids	"	.27	Foliage Spray	94% kill	Switzerland
Turnip	Myzus persicae	Greenhouse	.16	Soil	good control	U.S.
Brassicae	Brevicoryne brassicae	Field	.3	Foliage Spray	100% kill	U.K.
Beans (Vicia)	Aphis fabae	Laboratory	.05	Soil	96% "	U.K.
" (Phaseolus)	Tetranychus sp.	Greenhouse	.06	Foliage Spray	93% "	Holland
Peas	Macrosiphum pisi	"	.1	"	100% "	U.S.
Lettuce	Myzus persicae	Field	.4	"	96% "	U.S.
"	Pemphigus betae	"	.4	"	96% "	U.S.
"	Liriomyza orbona	"	.4	"	97% "	U.S.
Cotton	Aphis gossypii	Greenhouse	3.2	Soil	100% "	U.S.
"	Tetranychus bimaculatus	"	.05	Foliage Spray	97% "	U.S.
Hops	Tetranychus telarius	"	.075	"	good control	Germany
Hops	Phorodon humuli	Field	.075	"	100% kill	"
Sugar cane	Aphis sacchari	Greenhouse	.1	Soil	100% "	Mauritius
"	Mites	"	.1	"	93% "	"
Tobacco	Myzus persicae	"	.05	Foliage Spray	100% "	Italy
Auricula, Primula	Pemphigus auriculae	"	.33	Soil	100% "	U.K.
Carnation	Tetranychus telarius	"	.4	Foliage Spray	100% "	Holland
Chrysanthemum	Anuraphis helichrysi	"	.166	Soil	96% "	U.S.
"	Aphis gossypii	"	.166	"	96% "	"
"	Rhopalosiphum rufomaculatum	"	.166	"	96% "	"
"	Tetranychus bimaculatus	Field	.16	Foliage Spray	98% "	"
Tulips	Myzus persicae	Greenhouse	.2	Soil	100% "	U.K.
"	Macrosiphum gei	"	.2	"	100% "	U.K.
Rosa	Tetranychus bimaculatus	"	.166	"	94% "	U.S.

(1) Vs. Aphis gossypii, soil treatment at 4-8 lbs/acre, foliage treatment at 1 lb/acre: Eliminated insects. 1658

(2) Vs. Brevicoryne brassicae on Brussel's sprouts: at 3 lbs/acre in 0.2% H_2O solution yielded 70% control with protection for ca. 7 weeks; on hops at 1.5 lbs/acre gave complete control of Phorodon humuli for >6 weeks. 2655

(3) Vs. Pieris and Phyllodecta (chewing insects): No protection. 2202

(4) Vs. Brevicoryne brassicae: Excellent control by seed treatment (for a time;) excellent control for 2 months by watering young plants in seed flats before transplanting; solutions applied to base of new set plants yielded control to harvest; at 1.4-3 lbs/acre (sprays) gave excellent control for 50 days. 2595

(5) Vs. Macrosiphum pisi and Tetranychus atlanticus: Gave excellent control on alfalfa, with aphid control better on nearly mature than on rapidly growing plants. 2595

(6) Vs. Anuraphis tulipae: On carrots at 1.4 lbs/acre gave fair to good control. 2595

(7) Vs. Myzus persicae: Or sugar beets at 1.1-3.5 lbs/acre gave poor control. 2595

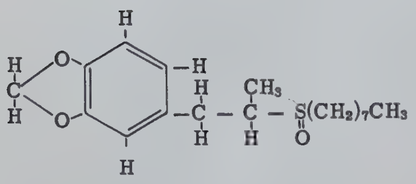
(8) Vs. Thrips tabaci: No control. 2595

(9) Vs. Tarsonemus pallidus: No control and no reduction at 2 lbs/acre. 2595

(10) Vs. Trialeurodes abutilonea: On cotton yielded no reduction in nymphs. 2595

133

n-OCTYL SULFOXIDE OF ISOSAFROLE (Sulfoxide®; Sulfox-Cide (formerly))



Molecular weight 324

GENERAL [Refs.: 3037,3040,1150,963,249]

A compound of negligible insecticidal properties per se but which acts as a potent synergist for pyrethrins, allethrin, and (?) rotenone. One of a category of organic substances with a methylene-dioxyphenyl group (among them being n-propyl isome, sesamin, piperonyl cyclonene and piperonyl butoxide q.v.) which contains many pyrethrum synergists. Sulfoxide® synergizes pyrethrins and allethrin to a significant degree, the synergistic action with pyrethrins being 4.7 times that with allethrin. A mixture of Sulfoxide® with pyrethrins at 5 to 1 is 10 times more toxic than the pyrethrins alone. A mixture of Sulfoxide® with allethrin at 5 to 1 is 2.32 times more toxic than allethrin alone. Taking into consideration the greater toxicity of allethrin toward Musca domestica (as compared with pyrethrins) and the synergistic effects, the relative effectiveness of mixtures of Sulfoxide® - pyrethrins is greater than that of mixtures of Sulfoxide® - allethrin.

PHYSICAL, CHEMICAL [Refs.: 3040,2542,3038,1061]

Technical: A brown liquid which may crystallize at low temperatures; decomposes on heating; $d^{25°}$ 1.07-1.08; $n_D^{25°}$ 1.529-1.532; virtually insoluble in water; low solubility (to 2.5%) in petroleum oils; soluble in many organic solvents.

a) Formulations: As such; as a solution at 40%, of which 35.5% is n-octyl sulfoxide of isosafrole and 4.9% is made up of related compounds; as an emulsifiable solution (Sulfoxide® + Pyrexcel® 1:10) with pyrethrins (Sulfoxide® 10.03%, pyrethrins 1.14%); as Sulfoxide® - Pyrexcel® 20 (pyrethrins 0.62%, Sulfoxide® 4.98%); with pyrethrins in aerosols generally at 1.0% Sulfoxide® and 0.2% pyrethrins.

TOXICOLOGICAL

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	ca2000		1951
Rabbit	ct	LD_{50}	> 9000	>9.0cc of the liquid.	1952

a) Administered in the diet of rats at 2000 ppm for 15 months, no deleterious effects were noted save a slight retard in weight gain. 2951

2) Phytotoxicity:

a) None reported in references studied for this compilation.

3) Toxicity for insects:

a) Mortality and "knockdown" of Musca domestica with various kerosene sprays of Sulfoxide®, Sulfoxide® + allethrin or pyrethrins and with allethrin or pyrethrins alone; application by the turntable method: 1150

Spray	Concentration (mg/cc)		% "Knockdown" In 25 Minutes	% Mortality 24 Hrs	Remarks
	Insecticide	Synergist			
Sulfoxide®	—	160	28	63.1	LC_{50} = 87.82 mg/cc; Rel. Stand. Error % = 4.67; Ratio toxicity to pyrethrins 0.01986 " " " allethrin 0.0075
"	—	80	28	48.4	
"	—	40	23	31.4	
"	—	20	32	22.2	
Pyrethrins	8	—	100	92.3	LC_{50} = 1.744 mg/cc; Rel. Stand. Error % = 8.76
"	4	—	100	82.8	
"	2	—	100	53.0	
"	1	—	100	30.2	
Allethrin	2	—	100	89.4	LC_{50} = 0.6591 mg/cc Rel. Stand. Error % = 7.9
"	1	—	100	64.1	
"	0.5	—	98	35.3	
"	.25	—	93	19.9	

a) Mortality and "knockdown" of Musca domestica with various kerosene sprays of Sulfoxide®, Sulfoxide® + allethrin or pyrethrins and with allethrin or pyrethrins alone; application by the turntable method: 1150

Spray	Concentration (mg/cc) Insecticide	Synergist	% "Knockdown" In 25 Minutes	% Mortality 24 Hrs	Remarks
Sulfoxide® + Pyrethrins	.5	25	100	94.9	Sulfoxide + Pyrethrins LC_{50} 0.7335 + 0.1467 mg/cc Rel. Stand. Error % = 8.48
"	.25	1.25	100	69.6	
"	.125	0.625	99.6	34.4	
"	.0625	0.313	95	22.7	
Sulfoxide® + Allethrin	1.0	5.0	100	97.0	Sulfoxide + Allethrin LC_{50} 1.369 + 0.2738 Rel. Stand. Error % 8.98
"	.5	2.5	99.7	79.4	
"	.25	1.25	98.6	40.8	
"	.125	0.625	73	14.4	

b) Effectiveness of Sulfoxide® as a synergist; in sprays vs. Musca domestica: 963

Material (mg/cc) in Deobase oil	% "Knockdown" In 5 min.	10 min.	% Mortality In 24 Hrs.
Pyrethrins 0.2 + Sulfoxide® 2.0	89	98	85
Pyrethrins 0.2 + Piperonyl butoxide 2.0	78	97	78
Pyrethrins 1.0 (alone)	92	97	37
Allethrin 0.2 + butylcellosolve 16 + Sulfoxide® 2.0	14	56	25
Allethrin 0.2 + butylcellosolve 16 + Piperonyl butoxide 2.0	10	54	34
Allethrin 1.0 (alone)	82	90	32

c) Comparative effectiveness of Sulfoxide® and piperonyl butoxide vs. Musca domestica in pyrethrum + DDT high pressure aerosols: 963

Synergist	% Knockdown In 5 min.	10 min.	15 min.	% Mortality In 24 Hrs.
		(At 0.35 g/1000 ft^3)		
Sulfoxide®	7	37	54	61
Piperonyl butoxide	10	23	32	37
		(At 1.16 g/1000 ft^3)		
Sulfoxide®	55	79	91	97
Piperonyl butoxide	54	81	89	94
		(At 0.37, 0.38 g/1000 ft^3)		
Sulfoxide®	24	65	82	81
No synergist	9	31	38	50

d) A sharp limitation of synergistic action is noted in the case of mosquitoes in flight through mists and of Sitophilus granarius crawling on oil film deposits, when pyrethrins + Sulfoxide® are present in equimolecular proportions. 249

134

ORGANIC PHOSPHATES (ORGANIC PHOSPHORUS [“ORGANOPHOSPHORUS”] INSECTICIDES)

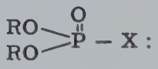
GENERAL [Refs.: 394,533,863,1725,2254,83,239,500,877,1272,1277,1342,1752,3230,3179,65,327,393,771,969, 1114,1245,1279,1334,1354,1438,1473,1515,3075,3076,161,2119,1755,14,2128,391,306,2,59,184,236, 773,1332,1844,2046,2273,2732,2941,3051,353,2231,2120,713,2773,2769,2771,2770,861,2053,1475, 326,2774,2775,2244,2245,509,2150,2651,864,505,1851,2340,851,713,32,858,30,794,1090,1801,59, 1281,1283,749,2054,301,302,2942,1659,1097,2076,2244,151,220,2126,1785,548,2864,1119,775,899, 1253,3365,2247,1130,1695,3257,714,237,497,703,704,1458,852,1584,2043,1121,672,1317,1316, 2768]

The designations used in the heading have been employed for a general category of toxicants. The members of this category are already numerous, and may become far more numerous since the possible number of structural variations and substitutions is almost unlimited. These arthropod toxicants include potent insecticides and acaricides; many of them have a high specificity of action, and others confer a“systemic” insecticidal activity on the tissues and juices of plants by which they are taken up after application at the roots or to the aerial parts. This insecticide and acaricide group is of recent introduction and is the subject of intense experimental interest in laboratory and field. Some compounds in the group have already taken their places among the commercial insecticides generally available to the farmer, gardener and husbandman. Discovered (as insecticides) in Germany in the last two decades, these compounds are being widely exploited. A general summary treatment for this group seems particularly valuable to indicate relationships between them and the several sub-groupings into which the members naturally fall. Generally speaking, a common mode of action has been attributed to the organic phosphate insecticides in insects, acarines and vertebrate animals, namely, the inhibition of certain esterases, notably choline esterase(s). All the toxicants of this group appear to share the property of inhibiting the action of choline esterase(s) in vivo and/or in vitro. Some of these compounds per se powerfully inhibit the esterase(s) in vivo and in vitro; others, relatively inactive against the esterase(s) in vitro, become by metabolic or other transformation in the plant, insect or vertebrate body, potent inhibitors in vivo.

In general, simple phosphoric acid esters of the types R-O-PO(OH)$_2$, (RO)$_2$ P-O-OH, (RO)$_3$ PO are only slightly (if at all) insecticidal. Insecticidal activity is shown when one of the R groups is acidic, for example, p-nitrophenyl and acetyl and in pyrophosphate types. In aromatic types (derivatives either of phosphoric or thiophosphoric acids) the benzene ring substituents are important. Activity is low in absence of substituents, high with para- or ortho- NO$_2$ (but not with meta- NO$_2$); Cl and methoxy- groups do not enhance activity markedly. Insertion of [-CH$_2$-] between the benzene ring and oxygen yields loss of insecticidal activity.

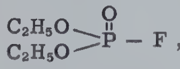
I) CLASSES OF ORGANIC PHOSPHORUS INSECTICIDES, AND COMPOUNDS EXEMPLIFYING THESE CLASSES, WHICH ARE OF KNOWN HIGH VALUE AS INSECT AND ACARINE TOXICANTS:

1) Halogenophosphates; group formula



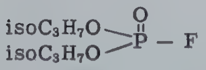
$\begin{matrix} RO \\ RO \end{matrix}\!>\overset{\overset{O}{\|}}{P} - X$:

a)



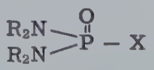
$\begin{matrix} C_2H_5O \\ C_2H_5O \end{matrix}\!>\overset{\overset{O}{\|}}{P} - F$, Diethyl fluorophosphate. 2769,2069

b)



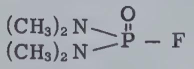
$\begin{matrix} isoC_3H_7O \\ isoC_3H_7O \end{matrix}\!>\overset{\overset{O}{\|}}{P} - F$, Di-isopropyl fluorophosphate (DFP). 2069,2150

2) Amidohalogenophosphates; group formula



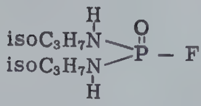
$\begin{matrix} R_2N \\ R_2N \end{matrix}\!>\overset{\overset{O}{\|}}{P} - X$:

a)



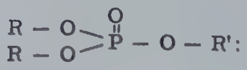
$\begin{matrix} (CH_3)_2\,N \\ (CH_3)_2\,N \end{matrix}\!>\overset{\overset{O}{\|}}{P} - F$, Bis-(dimethylamino) fluorophosphine oxide (BFPO). 2773,1467

b)



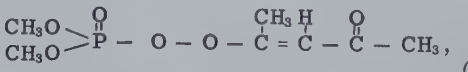
$\begin{matrix} isoC_3H_7\overset{H}{\overset{|}{N}} \\ isoC_3H_7\underset{H}{\underset{|}{N}} \end{matrix}\!>\overset{\overset{O}{\|}}{P} - F$, Bis-(monoisopropylamino) fluorophosphine oxide (Isopestox® .) 2651,2480,692

3) Orthophosphates; group formula

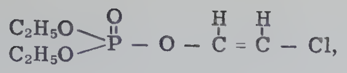


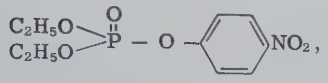
$\begin{matrix} R - O \\ R - O \end{matrix}\!>\overset{\overset{O}{\|}}{P} - O - R'$:

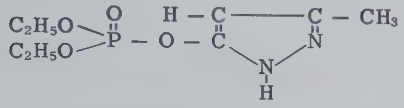
a)



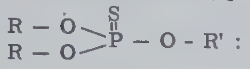
$\begin{matrix} CH_3O \\ CH_3O \end{matrix}\!>\overset{\overset{O}{\|}}{P} - O - O - \overset{\overset{CH_3}{|}}{C} = \overset{\overset{H}{|}}{C} - \overset{\overset{O}{\|}}{C} - CH_3$, O,O-Dimethyl O-1-carbomethoxy-1-propen-2-yl phosphate (Compound 2046 [Shell Chemical Corporation]). 2651 599

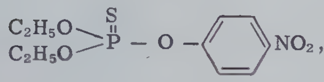
b) 
$\begin{matrix}C_2H_5O\\C_2H_5O\end{matrix}{>}\overset{O}{\overset{\|}{P}} - O - \overset{H}{\overset{|}{C}} = \overset{H}{\overset{|}{C}} - Cl$, O,O-Diethyl O-2-chlorovinyl phosphate (Compound 1836 [Shell Chemical Corporation]). 599, 600

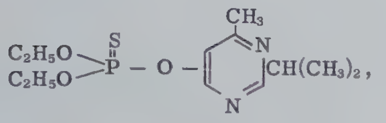
c)  O,O-Diethyl O-p-nitrophenyl phosphate (Para-oxon). 2769,3101,857

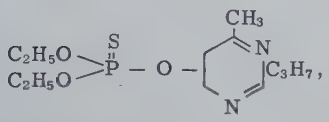
d)  O,O-Diethyl O-(3-methylpyrazolyl)-(5) phosphate (Pyrazoxon). 1387,1119

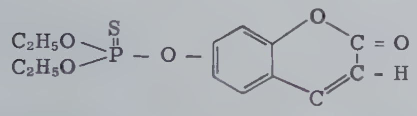
4) Orthothiophosphates (Phosphonothioates, phosphorothioates, phosphorothionates); group formula

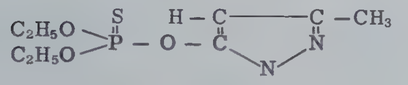

$$\begin{matrix}R-O\\R-O\end{matrix}{>}\overset{S}{\overset{\|}{P}} - O - R' :$$

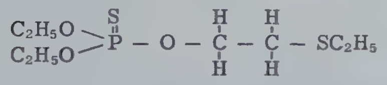
a)  O,O-Diethyl O-p-nitrophenyl thionophosphate (Parathion). 2128,2769 864,326

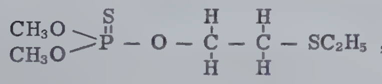
b)  O,O-Diethyl O-2-isopropyl-4-methylpyrimidyl-(6) thionophosphate (Diazinon). 1121

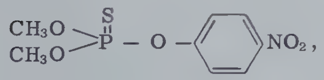
c)  O,O-Diethyl O-2-n-propyl-4-methylpyrimidyl-(6) thionophosphate (Pirazinon). 1123

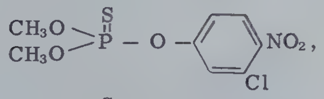
d)  O,O-Diethyl O-(4-methyl-7-coumarinyl) thionophosphate (Potasan®). 2773

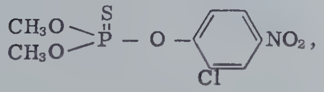
e)  O,O-Diethyl O-(3-methylpyrazolyl)-(5) thionophosphate (Pyrazothion). 1317

f) 
$\begin{matrix}C_2H_5O\\C_2H_5O\end{matrix}{>}\overset{S}{\overset{\|}{P}} - O - \underset{H}{\overset{H}{C}} - \underset{H}{\overset{H}{C}} - SC_2H_5$, O,O-Diethyl O-2-ethylmercaptoethyl thionophosphate (Systox®). 1468 2773 2651,1415

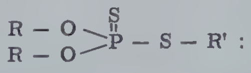
g) 
$\begin{matrix}CH_3O\\CH_3O\end{matrix}{>}\overset{S}{\overset{\|}{P}} - O - \underset{H}{\overset{H}{C}} - \underset{H}{\overset{H}{C}} - SC_2H_5$, O,O-Dimethyl O-2-ethylmercaptoethyl thionophosphate (Meta-Systox®). 2773

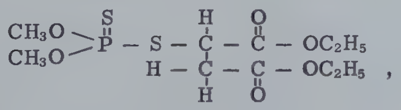
h)  O,O-Dimethyl O-p-nitrophenyl thionophosphate (Methyl parathion). 2773 1787,1783

i)  O,O-Dimethyl O-3-chloro-4-nitrophenyl thionophosphate (Chlorthion®). 2768,854

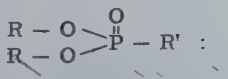
j)  O,O-Dimethyl O-2-chloro-4-nitrophenyl thionophosphate (Experimental Insecticide 4124 [American Cyanamid]). 2768

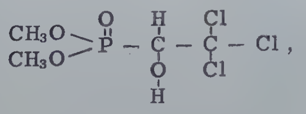
5) Dithiophosphates (phosphorodithioates); group formula

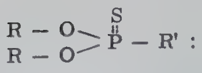

$$\begin{matrix}R-O\\R-O\end{matrix}{>}\overset{S}{\overset{\|}{P}} - S - R' :$$

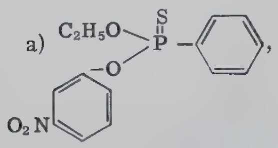
a) 
$\begin{matrix}CH_3O\\CH_3O\end{matrix}{>}\overset{S}{\overset{\|}{P}} - S - \overset{H}{C} - \overset{O}{\overset{\|}{C}} - OC_2H_5$ / $H - \underset{H}{C} - \underset{O}{\underset{\|}{C}} - OC_2H_5$, O,O-Dimethyl S-(1,2-dicarboethoxyethyl) di-thiophosphate (Malathion). 1709 1554 1461 1388

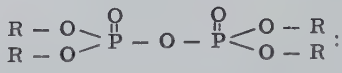
6) Phosphonates; group formula

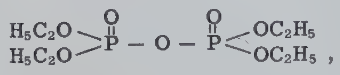

$$\begin{matrix}R-O\\R-O\end{matrix}{>}\overset{O}{\overset{\|}{P}} - R' :$$

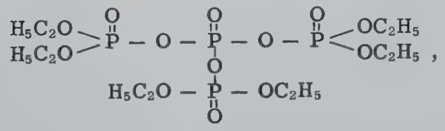
a) 
$\begin{matrix}CH_3O\\CH_3O\end{matrix}{>}\overset{O}{\overset{\|}{P}} - \underset{\underset{H}{O}}{\overset{H}{C}} - \underset{Cl}{\overset{Cl}{C}} - Cl$, O,O-Dimethyl 1-hydroxy-2-trichloromethyl phosphonate (Dipterex®). 196

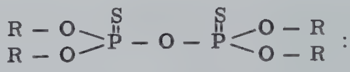
7) Thionophosphonates; group formula  $\begin{matrix}R-O\\R-O\end{matrix}\!>\overset{S}{\overset{\|}{P}}-R'$:

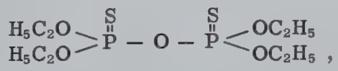
a)  O-Ethyl O-p-nitrophenyl benzene thionophosphonate (EPN®). 1692,1553 2248,2231,1953

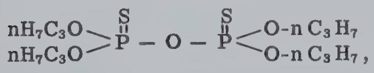
8) Pyrophosphates; group formula  $\begin{matrix}R-O\\R-O\end{matrix}\!>\overset{O}{\overset{\|}{P}}-O-\overset{O}{\overset{\|}{P}}\!<\begin{matrix}O-R\\O-R\end{matrix}$:

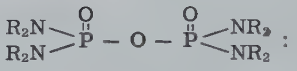
a)  $\begin{matrix}H_5C_2O\\H_5C_2O\end{matrix}\!>\overset{O}{\overset{\|}{P}}-O-\overset{O}{\overset{\|}{P}}\!<\begin{matrix}OC_2H_5\\OC_2H_5\end{matrix}$, Tetraethyl pyrophosphate (TEPP, Bladan). 2701,2702 1341,3104 3105,1339

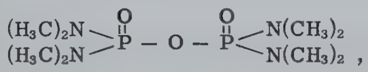
b)  $\begin{matrix}H_5C_2O\\H_5C_2O\end{matrix}\!>\overset{O}{\overset{\|}{P}}-O-\overset{O}{\overset{\|}{P}}-O-\overset{O}{\overset{\|}{P}}\!<\begin{matrix}OC_2H_5\\OC_2H_5\end{matrix}$, with $H_5C_2O-\overset{|}{\underset{\overset{\|}{O}}{P}}-OC_2H_5$ attached through O to the central P, Hexaethyl tetraphosphate (HETP). 2773,2775 1341

9) Dithionopyrophosphates; group formula  $\begin{matrix}R-O\\R-O\end{matrix}\!>\overset{S}{\overset{\|}{P}}-O-\overset{S}{\overset{\|}{P}}\!<\begin{matrix}O-R\\O-R\end{matrix}$:

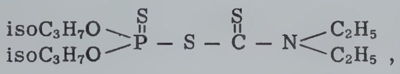
a)  $\begin{matrix}H_5C_2O\\H_5C_2O\end{matrix}\!>\overset{S}{\overset{\|}{P}}-O-\overset{S}{\overset{\|}{P}}\!<\begin{matrix}OC_2H_5\\OC_2H_5\end{matrix}$, Tetraethyl dithionopyrophosphate (Sulfatep). 2773,3106

b)  $\begin{matrix}nH_7C_3O\\nH_7C_3O\end{matrix}\!>\overset{S}{\overset{\|}{P}}-O-\overset{S}{\overset{\|}{P}}\!<\begin{matrix}O\text{-}n\,C_3H_7\\O\text{-}n\,C_3H_7\end{matrix}$, Tetra-n-propyl dithionopyrophosphate (NPD). 2773,3106

10) Pyrophosphoramides (pyrophosphoramidates); group formula  $\begin{matrix}R_2N\\R_2N\end{matrix}\!>\overset{O}{\overset{\|}{P}}-O-\overset{O}{\overset{\|}{P}}\!<\begin{matrix}NR_2\\NR_2\end{matrix}$:

a)  $\begin{matrix}(H_3C)_2N\\(H_3C)_2N\end{matrix}\!>\overset{O}{\overset{\|}{P}}-O-\overset{O}{\overset{\|}{P}}\!<\begin{matrix}N(CH_3)_2\\N(CH_3)_2\end{matrix}$, Octamethyl pyrophosphoramide (OMPA, Schradan) 2773,2653,554 705,3100,3101 1339,2651,141

11) Miscellaneous

a)  $\begin{matrix}isoC_3H_7O\\isoC_3H_7O\end{matrix}\!>\overset{S}{\overset{\|}{P}}-S-\overset{S}{\overset{\|}{C}}-N\!<\begin{matrix}C_2H_5\\C_2H_5\end{matrix}$, Diethyldithiocarbamic anhydride of O,O-di-isopropyl thionophosphoric acid (Holcomb Compound 326). 2120

II) STRUCTURE AND BIOLOGICAL ACTIVITY:

(N.B. This treatment is necessarily a summary; attention is called to the data given under the special treatment accorded each of the substances dealt with under I.)

a) Activity against insects and acarines:
(1) Toxicity of phosphorus acid esters for Myzus persicae; as contact sprays: 2053

Compound	R	Dilution	% Dead 24 Hrs (23.6% Difference for Significance At 5% level)	% Moribund	LC₅₀(%) Approximate
Alkyl acid phosphate esters $(HO)_2\overset{O}{\overset{\|}{P}}\text{-}OR$, $(HO)\overset{O}{\overset{\|}{P}}(OR)_2$		1:500			
Methyl	CH_3	"	51.4	3.1	
Ethyl	C_2H_5	"	37.8	6.6	>0.2
Propyl	C_3H_7	"	55.1	2.2	
Isopropyl	$(CH_3)_2CH$	"	73.6	1.9	
Butyl	C_4H_9	"	62.2	1.5	
Amyl	primaries	"	56.6	0.1	
Octyl	C_8H_{17}	"	79.4	0.4	
Loralkyl(s)	mixture 10-18 Carbons	"	4.5	0.3	
Trialkyl, triaryl esters $\overset{O}{\overset{\|}{P}}(OR)_3$					
Trimethyl	CH_3	"	52.2	5.7	
Triethyl	C_2H_5	"	14.7	6.5	>0.2
Tri-(β-chloroethyl)	$ClCH_2CH_2$	"	45.6	5.7	
Triallyl	$CH_2{=}CHCH_2$	"	28.8	3.9	
Trimethallyl	$CH_2{=}C(CH_3)CH_2$	"	33.9	3.6	
Tri-(2-ethyl hexyl)	$CH_3(CH_2)_3CH(C_2H_5)CH_2$	"	87.1	0.7	
Triphenyl	C_6H_5	"	21.2	4.3	

(1) Toxicity of phosphorus acid esters for Myzus persicae; as contact sprays: 2053

Compound	R		Dilution	% Dead 24 Hrs (23.6% Difference for Significance At 5% level)	% Moribund	LC_{50}(%) Approximate
Tri cresyl	$CH_3C_6H_4$		"	20.3	3.9	
Tri-(o-chlorophenyl)	ClC_6H_4		"	5.3	0.4	
Tri-(2,4,6-trichlorophenyl)	$Cl_3C_6H_2$		"	8.2	0.9	
Phosphonate esters $\overset{O}{\overset{\|}{P}}(R')(OR)_2$						
	R	R'	"			
Diethyl trichloromethane	C_2H_5	CCl_3	"	28.1	1.0	
Diethyl p-chlorobenzene	C_2H_5	ClC_6H_4	"	55.0	5.6	
Diethyl 3,4-dichlorobenzene	C_2H_5	$Cl_2C_6H_3$	"	66.8	4.0	
Dibutyl trichloromethane	C_4H_9	CCl_3	"	24.3	0.6	
Dibutyl 2-propene	C_4H_9	$CH_2{=}CHCH_3$	"	70.9	4.2	
" 2-methyl-2-propene	C_4H_9	$CH_2{=}C(CH_3)CH_2$	"	76.1	3.6	
" β-styrene	C_4H_9	$C_6H_5CH{=}CH$	"	90.3	4.3	
Di-(p-chlorophenyl)ethane	ClC_6H_4	C_2H_5	"	26.2	3.6	
Triethyl phosphonoacetate	C_2H_5	$C_2H_5OOCCH_2$	"	55.4	1.8	
Phosphite esters $P(OH)(OR)_2$, $P(OR)_3$						
Diethyl	C_2H_5		"	12.2	0	>0.2
Dibutyl	C_4H_9		"	23.8	2.5	
Triethyl	C_2H_5		"	13.7	0	>0.2
Tributyl	C_4H_9		"	30.6	0.5	
Aryl phosphonic acids $\overset{O}{\overset{\|}{P}}(OH)_2R$						
p-Chlorobenzene	ClC_6H_4		1:500	6.1	3.4	
3,4-Dichlorobenzene	$Cl_2C_6H_3$		"	4.8	1.2	
Phosphine oxides $\overset{O}{\overset{\|}{P}}R_3$						
Tri-(p-chlorophenyl)	ClC_6H_4		"	13.4	0.8	
Tri-(ethyl benzene phosphono)	$C_6H_5\overset{O}{\overset{\|}{P}}OC_2H_5$		"	94.6	1.7	

Toxicity of certain phosphorus acid esters for Myzus porosus; as contact sprays:

Compound	R	% Mortality (24 Hrs) At Dilution Shown*									
		1:500	1:1000	1:2000	1:4000	1:10,000	1:20,000	1:40,000	1:50,000	LC_{50}(%)Ca.	
Tetra-alkyl pyrophosphate esters $(RO)_2\overset{O}{\overset{\|}{P}}\text{-O-}\overset{O}{\overset{\|}{P}}(OR)_2$											
Tetraethyl	C_2H_5	—	—	—	—	—	95.4	85.6	52.7		0.0025
Tetrapropyl	C_3H_7	—	—	—	—	—	91.6	75.4	50.9		0.0025
Tetrabutyl	C_4H_9	—	—	—	—	—	71.3	—	—	91.2	<0.01
Tetraalkyl aryl triphosphate esters $(RO)_2\overset{O}{\overset{\|}{P}}\text{-O-}\overset{O}{\overset{\|}{P}}(OC_6H_5)O\overset{O}{\overset{\|}{P}}(OR)_2$											
Sym-Phenyl tetrapropyl	C_3H_7	—	—	—	—	—	85.9	66.4	—	—	—
Sym-Phenyl tetrabutyl	C_4H_9	—	—	94.3	—	45.1	—	—	—	—	—
Hexaethyl tetraphosphate esters $\overset{O}{\overset{\|}{P}}[O\overset{O}{\overset{\|}{P}}(OR)_2]_3$											
Hexaethyl	C_2H_5	—	—	—	—	88.8	63.4	—	—	—	0.01
Hexapropyl	C_3H_7	—	—	99.0	79.8	—	—	—	—		<0.025
Hexabutyl	C_4H_9	—	—	—	—	89.3	66.2	—	—		0.01
Hexa-(2-ethyl hexyl)		67.8	45.9	—	—	—	—	—	—		0.1
Nicotine Control (95% free base)		—	—	48.8	—	—	—	—	—		—

*Difference of 14.9%, 16%, 23.3% at 1:5000, 1:10,000, 1:20,000 dilutions required for significance at the 5% level.

(2) Comparative toxicities of certain organic phosphates in dipping tests: 301

Compound	Paratetranychus citri						Macrosiphum pisi (adult)		
	Adults, Nymphs			Eggs					
	ppm (v/v)	% Kill 24 hrs	LC_{50}ppm	ppm (v/v)	% Kill 7 days	LC_{50}ppm	ppm (v/v)	% Kill 24 hrs	LC_{50}ppm
Parathion	0.5	84	0.167	125	70	62.5	0.5	71	0.24
"	.25	63	—	62.5	48	—	.25	53	—
"	.1	33	—	31.25	35	—	.125	30	—
Tetraethyl pyrophosphate	1.0	93	0.37	62.5	64	3.125	2.0	67	1.28
"	.5	62	—	31.25	47	—	1.0	41	—
"	.25	32	—	15.6	39	—	.5	36	—
Tetra-isopropyl pyrophosphate	5.0	83	2.18	2500	65	940	50	71	32
"	2.5	53	—	1250	55	—	25	32	—
"	1.0	21	—	500	55	—	12.5	24	—

(3) Comparative toxicities of certain organic phosphorus insecticides used as dusts: 302

Insecticide	LC$_{50}$ (ppm) For			
	Macrosiphum pisi*	Phylactaenia rubigallis**	Oncopeltus fasciatus**	Paratetranychus citri***
EPN®	18.5	50	178	17.2
Methylethyl parathion	6.5	68	162	19.0
Methyl parathion	2.6	190	660	17.0
Parathion	5.0	76	125	19.8

*LC$_{50}$ 24 hrs; **LC$_{50}$ 48 hrs; ***LC$_{50}$ 72 hrs.

(4) Comparative toxicities of some organic phosphorus compounds as dusts, sprays: 301

Insect	% Mortality (48 Hrs) With																
	Parathion							Tetraethyl pyrophosphate					Tetraisopropyl pyrophosphate				
	Dust µg/cm^2				Spray ppm v/v			Dust µg/cm^2			Spray ppm v/v		Dust µg/cm^2			Spray ppm v/v	
	.16	.1	.28	.058	50	10	5	2.15	2.32	2.5	50	10	2.8	3.0	3.1	500	50
Altica ambiens	96	—	—	—	—	—	—	42	—	—	—	—	21	—	—	—	—
Cirphis unipuncta	—	100	—	—	100	—	—	—	100	—	46	—	—	13	—	88	—
Oncopeltus fasciatus	—	—	70	—	—	100	—	70	—	—	—	65	—	—	30	—	90
Tetranychus bimaculatus	—	—	—	87	—	—	96	—	—	100	—	96	14	—	—	—	87

(5) Activity of various organic phosphorus compounds vs. Periplaneta americana (adult ♂): (N.B. activity of ventral nerve cord cholinesterase of the adult ♂ roach: Average = 0.679 µ mole of acetylcholine split/mg tissue/hour.) 509

Compound	LD$_{50}$ (Injection) µg/g	Average Time (Hrs) For		% CHE Inhibition in vivo, Time Tested etc.
		Death	Symptoms	
Triethyl phosphate	$\gg$50	0*	0	38
Triethyl thiophosphate	15	50	1.5	98 (at 2xs the LD$_{50}$).
Diethyl monosodium phosphate	$\gg$50	0	0	—
Diethyl chlorophosphate	33.5	18-26	5-10 min.	99 (40 µg/g dose; 20 minutes after; 100% kill).
Diisopropyl chlorophosphate	$\gg$50	0	0	—
Diethyl thiochlorophosphate	19	ca50	ca 6	98 (30 µg/g dose; in 3 hours; 100% kill).
Ethyl thiodichlorophosphate	$\gg$50	0	0	—
Tetraethyl pyrophosphate †	3.0	23	12 min.	82 (1.6 µg/g dose; in 1 hour).
Diethyl p-nitrophenyl phosphate ††	0.7	ca18	15 min.	99 (1.0 µg/g dose; 100% kill).
Diethyl p-nitrophenyl thiophosphate †††	0.72	ca36	7 min.	100 (1.0 µg/g; in stage of paralysis**; 100% kill).
Diethyl p-aminophenyl thiophosphate HCl	8.0	45	6	99 (30 µg/g dose; 4 hrs after treatment).
Diethyl p-methoxyphenyl phosphate	$\gg$33	0	0	—
Diethyl p-nitrotolyl phosphate	$\gg$50	0	0	55 (9 hrs after 50 µg/g dose).
Diethyl p-chlorotolyl phosphonate	$\gg$50	0	0	—
Diethyl anilido phosphate	$\gg$50	0	0	—
Diisopropyl anilido phosphate	$\gg$50	0	0	51 (9 hrs after 50 µg/g dose).
Disodium p-nitrophenyl phosphate	$\gg$50	0	0	—
Di-(p-nitrophenyl)-p-chlorotolyl phosphate	$\gg$50	0	0	—

*O = does not kill, does not produce symptoms. **Tested in stage of total paralysis. † = TEPP, †† = Para-oxon, ††† = Parathion.

(6) Activity vs. Periplaneta americana (adult ♂): All values as molality x 10^{-4} ; toxic effects appear when in vivo CHE inhibition reaches 85%: 509

Compound	LD$_{50}$	ID$_{50}$ (in vitro) In		ID$_{50}$ (in vivo) In Time Given	
		1 hr.	4 hrs.		
Triethyl phosphate	$\gg$3.9 x 10^{-4}	5.5 x 10^{-4}	5.0 x 10^{-4}	>3.9 x 10^{-4}	in 8 hrs
Triethyl thiophosphate	1.09 "	.6 "	.045 "	<2.3 "	in 1 hr
Diethyl chlorophosphate	2.77 "	6.02 "	.02 "	<3.3 "	in 20 min.
Diethyl thiochlorophosphate	1.44 "	1.6 "	.5 "	<2.3 "	in 3 hrs
Tetraethyl pyrophosphate (TEPP)	0.14 "	0.018 "	.004 "	<0.079 "	in 15 min.
Diethyl p-nitrophenyl phosphate (Para-oxon)	0.039 "	0.018 "	.006 "	<0.055 "	in 30 min.
Diethyl p-nitrophenyl thiophosphate (Parathion)	0.037 "	—	5.0 "	0.05 "	in 3 hrs
Diethyl p-aminophenyl thiophosphate HCl	0.4 "	2.0 "	20.0 "	<1.5 "	in 3.5 hrs
Diethyl p-nitrotolyl phosphate	$\gg$0.26 "	—	—	2.6 "	in 9 hrs
Diisopropyl anilido phosphate	$\gg$0.25 "	—	—	2.8 "	in 9 hrs

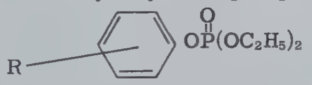
(7) Activity of various organic phosphorus compounds vs. Apis mellifera, and Musca domestica; average wgt.: Apis = 100 mg; Musca = 20 mg: 2244

Compound And Structural alteration	ID$_{50}$, For Apis Brain ChE in vitro	LD$_{50}$, Topical, (µg/g) For	
		Apis	Musca
Alteration of aliphatic group:			
Diethyl p-nitrophenyl phosphate (Para-oxon)	1.9 x 10^{-8} M	0.6	0.5
Diethyl p-nitrophenyl thiophosphate (Parathion)	1 x 10^{-6} M	3.5	0.9
Dimethyl p-nitrophenyl phosphate	4.2 x 10^{-8} M	0.3	1.0
Dimethyl p-nitrophenyl phosphate (Methyl parathion)	1.3 x 10^{-5} M	1.7	1.0
Di-isopropyl p-nitrophenyl phosphate	2.8 x 10^{-6} M	5	10.0
Di-isopropyl p-nitrophenyl thiophosphate	1.4 x 10^{-2} M	>1000	4.2
Di-propyl p-nitrophenyl thiophosphate	1.6 x 10^{-5} M	30	4.0
Ethyl butyl p-nitrophenyl thiophosphate	2 x 10^{-4} M	7	3.2
Bis-(dimethylamido)p-nitrophenyl phosphate	3 x 10^{-2} M	>1000	>500

(7) Activity of various organic phosphorus compounds vs. Apis mellifera, and Musca domestica; average wgt.: Apis = 100 mg; Musca = 20 mg: 2244

Compound And Structural alteration	ID$_{50}$, For Apis Brain ChE in vitro	LD$_{50}$, Topical, (μg/g) For Apis	LD$_{50}$, Topical, (μg/g) For Musca
Alteration of aromatic group:			
Diethyl phenyl phosphate	3×10^{-4} M	>1000	>500
Diethyl phenyl thiophosphate	3×10^{-3} M	>1000	>500
Diethyl o-nitrophenyl phosphate	3.3×10^{-7} M	1.0	7.0
Diethyl 2,4-dinitrophenyl phosphate	2.9×10^{-7} M	75.0	155
Diethyl p-chlorophenyl phosphate	4.2×10^{-4} M	> 100	150
Diethyl p-chlorophenyl thiophosphate	3.8×10^{-4} M	>1000	250
Diethyl o-chlorophenyl phosphate	5.7×10^{-5} M	> 100	250
Diethyl p-methylphenyl phosphate	6.2×10^{-6} M	200	>500
Diethyl p-methylphenyl thiophosphate	7.8×10^{-4} M	>1000	>500
Diethyl p-methoxyphenyl thiophosphate	3.2×10^{-4} M	>1000	>500
Diethyl p-tert.-butylphenyl phosphate	1.1×10^{-4} M	> 100	>500
Diethyl p-aminophenyl thiophosphate HCl	7.8×10^{-3} M	>1000	–
Diethyl 2-chloro-4-nitrophenyl thiophosphate	3×10^{-5} M	20	0.8
Diethyl 2-nitro-4-chlorophenyl phosphate	3.4×10^{-7} M	10	23
Diethyl 2-nitro-4-methylphenyl thiophosphate	1.1×10^{-4} M	>1000	450
Altered aromatic linkages:			
Diethyl p-nitrobenzyl thiophosphate	1.8×10^{-5} M	>1000	26
Diethyl p-nitrobenzyl dithiophosphate	2.2×10^{-5} M	>1000	21
Diethyl p-nitroanilido phosphate	1.0×10^{-4} M	> 100	>500
Phosphonic acid esters:			
Ethyl p-nitrophenyl benzene thiophosphonate (EPN®)	8.2×10^{-7} M	3.0	1.9
Diethyl benzene thiophosphonate	1.6×10^{-4} M	> 100	>500
Other aliphatic phosphate esters:			
Tetraethyl pyrophosphate (TEPP)	2.3×10^{-8} M	1.2	–
Tetraethyl dithiopyrophosphate (Sulfatep)	1.0×10^{-6} M	5.0	5.0
Octamethyl tetramido pyrophosphate (OMPA)	$>1.2 \times 10^{-3}$ M	> 100	>500

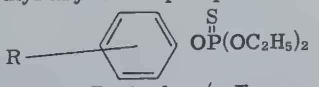
(8) Comparative toxicity of some diethyl aryl orthophosphates for several insects: 2231



(Group Formula)

R	LD$_{50}$ μg/g For Musca domestica (Topical)	LD$_{50}$ μg/g For Apis mellifera (Topical)	Apis mellifera ID$_{50}$, Brain ChE	LD$_{50}$ μg/g For Locusta migratoria (Injection)	Locusta migratoria ID$_{50}$, Nerve Cord ChE	LC$_{50}$ (%) As Contact Spray for Macrosiphum pisi
H	>500	>1000	3×10^{-4} M	–	–	–
p-CH$_3$	>500	200	6.2×10^{-5} M	–	–	–
p-(CH$_3$)$_3$C	>500	> 100	1.1×10^{-4} M	–	–	–
o-Cl	250	> 100	5.7×10^{-5} M	375	5×10^{-2} M	0.13
p-Cl	150	> 100	4.2×10^{-4} M	254	2×10^{-2} M	0.54
2,4-Di-Cl	–	–	–	25	4.2×10^{-4} M	0.078
2,4,5-Tri-Cl	–	–	–	3.2	7.5×10^{-6} M	0.015
o-NO$_2$	7	1	3.3×10^{-7} M	–	–	–
p-NO$_2$ (Para-oxon)	0.5	0.6	1.9×10^{-8} M	–	–	–
2,4-Di-NO$_2$	155	75	2.9×10^{-7} M	–	–	–
2NO$_2$,4Cl	23	10	3.4×10^{-7} M	–	–	–

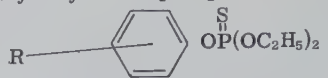
(9) Comparative toxicity of some diethyl aryl thionophosphates for insects and mouse: 2231



(Group Formula)

R	Toxic Level For Aphids (% Conc.)	LD$_{50}$, Topical μg/g For Musca domestica	LD$_{50}$, Topical μg/g For Apis mellifera	Toxic Dose, Sub-cutaneous (mg/k) For Mouse
H	0.2 - 0	>500	>1000	500
p-Cl	0.2 - 60	250	>1000	500
m-Cl	0.2 - 30	–	–	500
o-Cl	0.2 - 0	–	–	500
p-NO$_2$ (Parathion)	0.001-100	0.9	3.5	18
m-NO$_2$	0.05 -100	–	–	100-150
o-NO$_2$	0.01 -100	–	–	50

(9) Comparative toxicity of some diethyl aryl thionophosphates for insects and mouse (Continued): 2231


(Group Formula)

R	Toxic Level For Aphids (% Conc.)	LD$_{50}$, Topical µg/g For Musca domestica	LD$_{50}$, Topical µg/g For Apis mellifera	Toxic Dose, Sub-cutaneous (mg/k) For Mouse
p-CH_3	—	>500	>1000	—
p-CH_3O	—	>500	>1000	—
p-CN	0.05-100		—	75
p-NH_2Cl	—	—	>1000	—
p-C_2H_5OOC	0.2 - 0	—	—	200
o-C_2H_5OOC	0.2 - 0	—	—	250
m-C_2H_5OOC	0.2 - 0	—	—	300
2-C_2H_5OOC, 4-NO_2	0.2 - 0	—	—	100
2-CH_3, 4-SCN	0.2 - 0	—	—	1000
3-SCN, 5-CH_3	0.2 - 90	—	—	1000
2-Cl, 4-NO_2	—	0.8	20	—
2-NO_2, 4-Cl	—	9	30	—
2-NO_2, 4-CH_3	—	450	>1000	—

(10) Toxicity of parathion and parathion-related substances for certain aphids: 2769

Compound	% Concentration As Contact Spray To Yield 50% Mortality	% Concentration As Contact Spray To Yield 100% Mortality
O,O-Diethyl-O-p-nitrophenyl thiophosphate (Parathion)	—	0.001
" " " -phenyl phosphate	0.2	—
" " " -phenyl thiophosphate	0.2	—
" " " p-nitrophenyl phosphate (Para-oxon)	0.001	0.005
" " "o- " "	—	0.005
" " "m- " "	ca0.2	—
O-Ethyl-N(dimethylamido)-O-p-nitrophenyl phosphate	0.2	—
N,N-Bis (") "-" " "	0.05	—
O-Ethyl O-o-nitrophenyl methane phosphonate	0.005	0.05
O-Ethyl O-phenyl methane phosphonate	0.05	
O,O-Diethyl O-o-chlorophenyl phosphate	0.05	0.2
" " " "-p- " "	0.02	0.2
O-Propyl-O-2,4-dinitro phenylmethane phosphonate	—	0.2
O-Ethyl-O-2-nitro-4-methyl phenyl methane phosphonate	—	0.005
" " "-o-chlorophenyl methane phosphonate	—	0.05
O-Propyl-O-p- " "	—	0.2
O-Ethyl-O-p-carboethoxy methane phosphonate	—	0.05
O,O-Diethyl O-o-carboethoxy phosphate	—	0.05
N,N-Bis-(dimethylamido)-O-p-aminophenyl phosphate	> 0.2	—
" " " (")-"-o- " "	> 0.2	—

(11) Comparative activity of several organic phosphorus compounds, tested against certain insects and the laboratory mouse: 2245

Compound	ID$_{50}$ in vitro At 37°C For Brain ChE Of Musca domestica ((X) x 10^{-X} M)	ID$_{50}$ in vitro At 37°C For Brain ChE Of Apis mellifera	ID$_{50}$ in vitro At 37°C For Brain ChE Of Mouse	LD$_{50}$ (mg/k) For Musca (topical)	LD$_{50}$ (mg/k) For Apis (topical)	LD$_{50}$ (mg/k) For Mouse (oral)
Para-oxon	2.6 x 10^{-8}	1.9 x 10^{-8}	1 x 10^{-7}	0.5	0.6	3
Parathion	4.5 x 10^{-7}	1 x 10^{-6}	2.5 x 10^{-6}	0.9	3.5	6
Diisopropyl p-nitrophenyl thiophosphate	2 x 10^{-5}	1.4 x 10^{-2}	>1 x 10^{-2}	4.2	>1000	>100*
Di-n-propyl p-nitrophenyl thiophosphate	5 x 10^{-6}	1.6 x 10^{-5}	3 x 10^{-5}	4	30	>100*
EPN®	3 x 10^{-7}	8.2 x 10^{-7}	1.5 x 10^{-5}	1.9	3	50-100
Tetraisopropyl pyrophosphate	1 x 10^{-7}	1.5 x 10^{-5}	2 x 10^{-5}	6.5	23	50-100
Tetraisopropyl dithiopyrophosphate	3 x 10^{-6}	3 x 10^{-4}	1.5 x 10^{-3}	30	1000	>200*
Tetra-n-propyl dithiopyrophosphate	5 x 10^{-7}	3 x 10^{-6}	5 x 10^{-5}	15	200	>200*
Diisopropyl fluorophosphonate	1.3 x 10^{-8}	2 x 10^{-7}	8 x 10^{-8}	15	30	37

*Solubility in propylene glycol limited.

b) Toxicity of organic phosphate insecticides for insects; quantitative summary:

Insecticide	Insect	Route	Dose	Dosage	
Bayer 21/199	Anopheles quadrimaculatus (larva)	Medium	LC$_{100}$	ca0.025 ppm	1766
" "	" " "	Medium	LC$_{100}$	ca0.05 lbs/acre	1766
" "	Chrysops discalis (adult)	Topical	LD$_{90}$	90 µg/fly	2707
" "	" " "	Topical	LD$_{90}$	910 µg/fly	2707
Bayer 17147	Heliothis virescens (larva 6th I)	Topical	LD$_{50}$	54 µg/g	1124
" "	Heliothis zea (larva 6th I)	Topical	LD$_{50}$	40 µg/g	1124
BFPO (Dimefox)	Apis mellifera (adult)	or	LD$_{20}$ 24 hrs	1.25 µg/bee	1718
" "	" " "	or	LD$_{50}$ 24 hrs	1.905 µg/bee	1718
" "	" " "	or	LD$_{90}$ 24 hrs	3.506 µg/bee	1718

b) Toxicity of organic phosphate insecticides for insects; quantitative summary:

Insecticide	Insect	Route	Dose	Dosage	
BFPO (Dimefox)	Apis mellifera (adult)	Contact Spray	LD$_{20}$	16.52 µg/cm^2	1718
" "	" " "	Contact Spray	LDeposit$_{50}$	23.17 µg/cm^2	1718
" "	" " "	Contact Spray	LDeposit$_{90}$	38.64 µg/cm^2	1718
Chlorthion®	Anopheles quadrimaculatus (larva)	Medium	LC$_{100}$	ca0.05 ppm	1766
"	" " "	Medium	LC$_{100}$	ca 0.25 Lbs/acre	1766
"	Chrysops discalis (adult)	Topical	LD$_{50}$	65 µg/fly	2707
"	" " "	Topical	LD$_{90}$	420 µg/fly	2707
"	Fannia canicularis (adult)	Topical	LD$_{50}$ 24 hrs	♀ 0.035; ♂ 0.022 µg/fly	1981
"	Musca domestica (adult) ♀	Topical	LD$_{50}$ 24 hrs	0.33 µg/fly	1981
"	" " "	Topical	LD$_{50}$	16.5 µg/g	2231
Diazinon	Anopheles quadrimaculatus (larva)	Medium	LC$_{100}$ 48 hrs	0.01-0.1 ppm	1766
"	" " "	Medium	LC$_{100}$	ca0.1 Lb/acre	1766
"	Chrysops discalis (adult)	Topical	LD$_{50}$	90 µg/fly	2707
"	" " "	Topical	LD$_{90}$	360 µg/fly	2707
"	Fannia canicularis (adult)	Topical	LD$_{50}$ 24 hrs	♀ 0.098; ♂ 0.054 µg/fly	1981
"	Musca domestica (adult ♀)	Topical	LD$_{50}$ 24 hrs	0.092 µg/fly	1981
"	" " "	Topical	LD$_{50}$	4.6 µg/g	2231
Dipterex® (Bayer 13/59)	Heliothis virescens (larva, 6th I)	Topical	LD$_{50}$	60.0 µg/g	1124
" "	Heliothis zea (larva, 6th I)	Topical	LD$_{50}$	30.0 µg/g	1124
" "	Musca domestica (adult)	Topical	LD$_{50}$	0.0315 µg/fly	150
DFP	Apis mellifera (adult)	Topical		30 µg/g	2231
"	Musca domestica (adult)	Topical		15 µg/g	2231
EPN®	Anopheles quadrimaculatus (larva)	Medium	LC$_{100}$	0.0025-0.005 ppm	1766
"	" " "	Medium	LC$_{100}$	0.005-0.05 Lb/acre	1766
"	Aëdes nigromaculis (larva)	Medium	LC$_{50}$ 24 hrs	0.000862 ppm	1193
"	Apis mellifera (adult)	Topical	LD$_{50}$	3.0 µg/g	2231
"	Chrysops discalis (adult)	Topical	LD$_{50}$	48 µg/fly	2707
"	" " "	Topical	LD$_{90}$	120 µg/fly	2707
"	Conotrachelus nenuphar (adult)	Topical	LC$_{50}$	32 ppm	2864
"	" " "	Residues	Min. Effective Residue 68 mg/100cm^2		2864
"	Culex tarsalis (larva)	Medium	LC$_{50}$ 24 hrs	0.000649 ppm	1193
"	Musca domestica (adult)	Topical	LD$_{50}$ 24 hrs	1.9 µg/g	2247,2231
HETP	Melanoplus differentialis (adult)	Topical	LD$_{50}$	18.4 µg/g	3267
"	Musca domestica (adult)	Contact Spray	LC$_{50}$	0.52 ± .05 mg/cc	1164
Isopropyl parathion	Musca domestica (adult)	Topical	LD$_{50}$ 24 hrs	4.8 µg/g	2247
Malathion	Anopheles quadrimaculatus (larva)	Medium	LC$_{100}$ 48 hrs	0.05-0.1 ppm	1766
"	" " "	Medium	LC$_{90}$ 24 hrs	ca0.25 Lb/acre	1766
"	" " (adult)	Topical	LD$_{50}$	♂ 0.0087; ♀ 0.0095 µg/insect	2051
"	" " "	Topical	LD$_{90}$	♂ 0.019; ♀ 0.022 µg/insect	2051
"	Aëdes nigromaculis (larva)	Medium	LD$_{50}$ 24 hrs	0.025 ppm	1193
"	Caitophorus populi	Contact Spray	LC$_{50}$	0.022 g/l	775
"	Chrysops discalis (adult)	Topical	LD$_{50}$	130 µg/fly	2707
"	" " "	Topical	LD$_{90}$	330 µg/fly	2707
"	Culex tarsalis (larva)	Medium	LC$_{50}$	0.0185 ppm	1193
"	Ephestia kühniella (larva)	Contact Spray	LC$_{50}$	> 4 g/l	775
"	Fannia canicularis (adult)	Topical	LD$_{50}$ 24 hrs	♀ 0.1; ♂ 0.06 µg/fly	775
"	Heliothis virescens (larva 6th I)	Topical	LD$_{50}$	160 µg/g	1124
"	H. zea (larva 6th I)	Topical	LD$_{50}$	130 µg/g	1124
"	Musca domestica (adult) ♀	Topical	LD$_{50}$ 24 hrs	0.56 µg/fly	1981
"	" " "	Contact Spray	LC$_{50}$ 24 hrs	0.48 mg/cc	2033
"	" " "	Contact Spray	LC$_{50}$	0.74 g/l	775
"	" " "	Topical	LD$_{50}$	28 µg/g	2231,2247
"	Myzus persicae	Contact Spray	LC$_{50}$	0.03; 0.098 g/l	775
"	Protoparce sexta (larva 5th I)	Topical	LD$_{50}$	481 µg/larva	1306
"	" " (" 3,4 I)	Topical	LD$_{50}$	61 µg/larva	1306
"	" " (" 2,3 I)	Topical	LD$_{50}$	23.6 µg/larva	1306
"	" " (" 5th I)	Topical	LD$_{90}$	1276 µg/larva	1306
"	" " (" 3,4 I)	Topical	LD$_{90}$	553 µg/larva	1306
"	" " (" 2,3 I)	Topical	LD$_{90}$	92 µg/larva	1306
"	" " (" 5th I)	or	LD$_{50}$	355 µg/larva	1306
"	" " "	or	LD$_{90}$	1621 µg/larva	1306
"	Sitophilus granarius (adult)	Contact Spray	LC$_{50}$	0.092; 0.088 g/l	775
"	Tenebrio molitor (larva)	Contact Spray	LC$_{50}$	> 1.6 g/l	775
"	Tetranychus bimaculatus	Contact Spray	LC$_{50}$	0.049 g/l	775
"	Tribolium confusum (adult)	Contact Spray	LC$_{50}$	0.42; 0.53 g/l	775
Methyl parathion	Anopheles quadrimaculatus (larva)	Medium	LC$_{100}$ 48 hrs	0.005-0.01 ppm	1766
" "	" " "	Medium	LC$_{100}$ 24 hrs	0.05-0.1 Lb/acre	1766
" "	Locusta migratoria (adult)	Topical	LD$_{50}$ 96 hrs	0.94 ± 0.1 µg/insect	1585
" "	" " "	Topical	LD$_{50}$ 96 hrs	0.89 µg/g	1585
" "	" " "	Topical	LD$_{95}$ 96 hrs	2.3 ± 0.52 µg/insect	1585
" "	" " "	Topical	LD$_{95}$ 96 hrs	2.2 µg/g	1585
" "	Apis mellifera (adult)	Topical	LD$_{50}$	1.7 µg/g	2231
" "	Musca domestica (adult)	Topical	LD$_{50}$	1.0 µg/g	2231
" "	" " "	Topical	LD$_{50}$ 24 hrs	1.3 µg/g	2247
" "	" " "	Contact Spray	LC$_{50}$ 24 hrs	0.025 mg/cc	2033
NPD	Anopheles quadrimaculatus (larva)	Medium	LC$_{50}$ 48 hrs	ca0.025 ppm	1766
"	" " "	Medium	LC$_{100}$ 24 hrs	0.1-0.25 Lb/acre	1766
"	Aëdes nigromaculis (larva)	Medium	LC$_{50}$ 24 hrs	0.0625 ppm	1193
"	Apis mellifera (adult)	Topical	LD$_{50}$	200 µg/g	2231
"	Culex tarsalis (larva)	Medium	LC$_{50}$ 24 hrs	0.0178 ppm	1193
"	Musca domestica (larva)	Topical	LD$_{50}$	15 µg/g	2231
"	" " "	Contact Spray	LC$_{50}$ 24 hrs	0.69 mg/cc	2033
OMPA (Schradan)	Aëdes aegypti (larva)	Medium	LC$_{50}$	0.29 ppm	672
" "	" " "	Medium	LC$_{90}$	0.95 ppm	672
" "	Anasa tristis (adult)	Topical	LD$_{50}$	16 µg/g	2392
" "	Apis mellifera (adult)	Topical	LD$_{50}$	> 1000 µg/g	2244
" "	Lachnus saligenus	Topical	LD$_{50}$	22 µg/g	878
" "	Musca domestica (adult)	Topical	LD$_{50}$	> 500 µg/g	2244
" "	Oncopeltus fasciatus (adult)	Topical	LD$_{50}$	ca30 µg/g	2392
" "	Periplaneta americana (adult)	Topical	LD$_{50}$	> 100 µg/g	2244

b) Toxicity of organic phosphate insecticides for insects; quantitative summary:

Insecticide	Insect	Route	Dose	Dosage	
OMPA (Schradan)	Periplaneta americana (adult)	Injection	LD_{50}	> 100 μg/g	2244
" "	Phormia regina	Injection	LD_{50}	175 μg/g	2392
" "	Pyrrhocoris apterus	Topical	LD_{50}	34 μg/g	878
" "	Tenebrio molitor (larva)	Injection	LD_{50}	> 100 μg/g	2392
" "	Peregrinus maidis (adult)	Contact Spray	LC_{50} 24 hrs	0.58 (.569-.592) mg/cc	3181
" "	Cyrtorhinus mundulus (adult)	Contact Spray	LC_{50} 24 hrs	1.733 (1.578-1.990) mg/cc	3181
" "	Vanessa antiopa (larva)	Injection	LD_{50}	> 400 μg/g	2392
Para-oxon	Aëdes aegypti (larva)	Medium	LC_{50}	0.007 ppm	672
" "	" " "	Medium	LC_{90}	0.016 ppm	672
" "	Anopheles quadrimaculatus (larva)	Medium	LC_{100} 48 hrs	0.025 ppm	1766
" "	" " "	Medium	LC_{90}	0.1 Lb/acre	1766
" "	Apis mellifera (adult)	Topical	LD_{50}	0.6 μg/g	2231
" "	Musca domestica (adult)	Topical	LD_{50}	0.5 μg/g	2231
" "	Periplaneta americana (adult)	Topical	LD_{50}	0.75 μg/g	2231
" "	" " "	Injection	LD_{50}	0.65 μg/g	2231
Parathion	Anopheles quadrimaculatus (larva)	Medium	LC_{100} 48 hrs	0.005 ppm	1766
"	" " "	Medium	LC_{100} 24 hrs	ca0.05 Lb/acre	1766
"	Aphis rumicis	Topical	LD_{50}	0.0005 μg/insect	1119
"	" "	Topical	LD_{50}	0.8 μg/g	1119
"	Apis mellifera (adult)	or	LD_{50}	0.1 μg/insect, 1.0 μg/g	1119
"	" " "	Topical	LD_{50}	1.47 μg/g	206
"	" " "	Topical	LD_{95}	1.67 μg/g	206
"	" " "	or	LD_{50}	0.08 μg/g	206
"	" " "	or	LD_{95}	0.2 μg/g	206
"	" " "	Injection	LD_{50}	0.94 μg/g	206
"	" " "	Injection	LD_{95}	3.47 μg/g	206
"	" " "	or	LD_{20} 24 hrs	0.018 μg/bee	1718
"	" " "	or	LD_{50} 24 hrs	0.04 μg/bee	1718
"	" " "	or	LD_{90} 24 hrs	0.144 μg/bee	1718
"	" " "	Contact Spray	LD_{20}	0.257 μg/cm^2	1718
"	" " "	Contact Spray	LD_{50}	0.354 μg/cm^2	1718
"	" " "	Contact Spray	LD_{90}	0.574 μg/cm^2	1718
"	" " "	Residues	$LDeposit_{90}$	0.54 μg/cm^2	1718
"	" " "	Fumigant	$LDeposit_{100}$	5.0 μg/cm^2	1718
"	" " "	or	LD_{50} 72 hrs	0.07 μg/bee	910
"	" " "	or	LD_{50} 24 hrs	0.09 μg/bee	2729
"	" " "	or	LD_{50}	0.1 μg/bee	1330
"	Caitophorus populi	Contact Spray	LC_{50}	0.008 g/l	775
"	Cirphis unipuncta (larva)	Topical	LD_{50}	3.7 μg/g	3268
"	" " "	or	LD_{50}	2.5 μg/g	3268
"	Conotrachelus nenuphar (adult)	Topical	LC_{50}	14 ppm	2864
"	" "	Min. Eff. Residue		34 mg/100 cm^2	2864
"	Dacus dorsalis (adult)	Topical	LD_{50}	0.015 μg/fly	2692
"	Diataraxia oleracea (larva 0.32g)	or	LD_{50}	2.6 μg/larva	3245
"	" " (" 0.42g)	or	LD_{50}	3.4 μg/larva	3245
"	" " (" 0.56g)	or	LD_{50}	4.6 μg/larva	3245
"	Ephestia kühniella (larva)	Contact Spray	LC_{50}	0.21 g/l	775
"	" " "	or	LD_{50}	0.01 μg/insect, 1.0 μg/g	1119
"	Galleria mellonella	Topical	LD_{50}	2215 μg/g	206
"	" "	Topical	LD_{95}	24,200 μg/g	206
"	Melanoplus differentialis (adult)	Topical	LD_{50}	0.7; 0.8 μg/g	3267
"	" " "	or	LD_{50}	6.0; 8.9 μg/g	3267
"	Musca domestica (adult)	Topical	LD_{50}	0.015 μg/fly	2692
"	" " "	Topical	LD_{50}	0.9 μg/g	2231
"	" " "	Topical	LD_{50} 24 hrs	1.4 μg/g	2247
"	" " "	Contact Spray	LC_{50} 24 hrs	0.02 mg/cc	2033
"	" " "	Contact Spray	LC_{50}	0.03 ± 0.003 mg/cc	1164
"	" " "	Contact Spray	LC_{50}	0.032 g/l	775
"	" " "	or	LD_{50}	0.01 μg/fly, 0.5 μg/g	1119
"	Myzus persicae	Contact Spray	LC_{50}	0.0125; 0.021 g/l	775
"	Oncopeltus fasciatus	Topical	LD_{50}	47 μg/g	206
"	" "	Topical	LD_{95}	140 μg/g	206
"	" "	Injection	LD_{50}	8.39 μg/g	206
"	" "	Injection	LD_{95}	28.3 μg/g	206
"	Galleria mellonella	or	LD_{50}	125 μg/g	206
"	" "	or	LD_{95}	532 μg/g	206
"	" "	Injection	LD_{50}	91.1 μg/g	206
"	" "	Injection	LD_{95}	3706 μg/g	206
"	Popillia japonica	Topical	LD_{50}	3.3 μg/g	206
"	" "	Topical	LD_{95}	27.8 μg/g	206
"	" "	or	LD_{50}	4.51 μg/g	206
"	" "	or	LD_{95}	23.0 μg/g	206
"	" "	Injection	LD_{50}	0.448 μg/g	206
"	" "	Injection	LD_{95}	5.79 μg/g	206
"	Periplaneta americana (adult)	Topical	LD_{50}	1.2 μg/g	2231
"	" " "	Injection	LD_{50}	0.95 μg/g	2231
"	Plusia gamma	or	LD_{50}	2.5 μg/insect	1119
"	" "	or	LD_{50}	7.5 μg/g	1119
"	Protoparce sexta (larva 5th I)	Topical	LD_{50}	52 μg/larva	1306
"	" " "	Topical	LD_{90}	183 μg/larva	1306
"	" " (larva 3,4 I)	Topical	LD_{50}	9.9 μg/larva	1306
"	" " (" 3,4 I)	Topical	LD_{90}	64 μg/larva	1306
"	" " (" 2,3 I)	Topical	LD_{50}	2.8 μg/larva	1306
"	" " "	Topical	LD_{90}	12.3 μg/larva	1306
"	" " (larva 5th I)	or	LD_{50}	15.7 μg/larva	1306
"	" " "	or	LD_{90}	54 μg/larva	1306
"	Rhagoletis completa (adult)	Topical	LD_{50}	0.011 μg/fly	2692
"	Sitophilus granarius (adult)	Contact Spray	LC_{50}	0.031; 0.044 g/l	775
"	Tenebrio molitor (larva)	Contact Spray	LC_{50}	0.165 g/l	775
"	Tetranychus bimaculatus	Contact Spray	LC_{50}	0.02 g/l	775
"	Tribolium confusum (adult)	Contact Spray	LC_{50}	0.031; 0.046 g/l	775

b) Toxicity of organic phosphate insecticides for insects; quantitative summary:

Insecticide	Insect	Route	Dose	Dosage	
Potasan®	Anopheles quadrimaculatus (larva)	Medium	LC$_{100}$ 48 hrs	0.05-0.1 ppm	1766
Sulfatep	A. quadrimaculatus (larva)	Medium	LC$_{100}$ 48 hrs	0.0025 ppm	1766
"	" " "	Medium	LC$_{85}$ 24 hrs	0.1 Lb/acre	1766
"	Apis mellifera (adult)	Topical	LD$_{50}$	5.0 µg/g	2231
"	Musca domestica (adult)	Topical	LD$_{50}$	5.0 µg/g	2231
TEPP	Apis mellifera (adult)	Topical	LD$_{50}$	1.2 µg/g	2231
"	" " "	or	LD$_{50}$ 72 hrs	0.75 µg/bee	910
"	" " "	or	LD$_{20}$	0.052 µg/bee	1718
"	" " "	or	LD$_{50}$	0.065 µg/bee	1718
"	" " "	or	LD$_{90}$	0.093 µg/bee	1718
"	" " "	Contact Spray	LDeposit$_{20}$	0.358 µg/cm^2	1718
"	" " "	Contact Spray	LDeposit$_{50}$	0.445 µg/cm^2	1718
"	" " "	Contact Spray	LDeposit$_{90}$	0.621 µg/cm^2	1718
"	Diataraxia oleracea (larva, 0.32g)	or	LD$_{50}$	43 µg/larva	3245
"	" " (" , 0.42g)	or	LD$_{50}$	69 µg/larva	3245
"	" " (" , 0.56g)	or	LD$_{50}$	112 µg/larva	3245
"	Melanoplus differentialis (adult)	Topical	LD$_{50}$	4.4 µg/g	3267
"	Musca domestica (adult)	Contact Spray	LC$_{50}$ 24 hrs	0.069 mg/cc	2033
"	" " "	Contact Spray	LC$_{50}$ 24 hrs	0.095 ± .01 mg/cc	1164
"	Periplaneta americana (adult)	Injection	LD$_{50}$	3.0 µg/g	2231
Systox® (Demeton)	Apis mellifera (adult)	or	LD$_{20}$ 24 hrs	1.256 µg/bee	1718
" "	" " "	or	LD$_{50}$ 24 hrs	1.478 µg/bee	1718
" "	" " "	or	LD$_{90}$ 24 hrs	1.884 µg/bee	1718
" "	" " "	Contact Spray	LDeposit$_{20}$	4.32 µg/cm^2	1718
" "	" " "	Contact Spray	LDeposit$_{50}$	5.12 µg/cm^2	1718
" "	" " "	Contact Spray	LDeposit$_{90}$	6.62 µg/cm^2	1718
" "	" " "	Residues	LDeposit$_{50}$	0.01 mg/cm^2	1718
" "	" " "	Residues	LDeposit$_{20}$	0.0068 mg/cm^2	1718
" "	Cyrtorhinus mundulus (adult)	Contact Spray	LC$_{50}$ 24 hrs	0.037 (0.031-0.044) mg/cc	3181
" "	Peregrinus maidis (Adult)	Contact Spray	LC$_{50}$ 24 hrs	0.044 (0.041-0.046) mg/cc	3181

c) Some miscellaneous evaluations of toxicity of various organic phosphorus compounds for insects:

(1) Comparative affectiveness of ethyl and methyl homologues, evaluated against 4 pests of cotton: 1659,1097

Compound	Lbs/Acre To Yield Indicated Net Mortality For								
	Anthonomus grandis		Aphis gossypii		Septanychus desertorum		Alabama argillacea		
	50%	90%	50%	90%	50%	90%	50%	90%	
O,O-Diethyl-O-p-nitrophenyl thiophosphate	0.15	0.413	0.022	0.143	0.081	0.640	0.002	0.523	Parathion
O,O-Dimethyl- " "	.011	.176	.013	.102	.316	1.58	.051	.188	Methyl parathion
O,O-Diethyl O-4-methyl umbelliferone thiophosphate	.165	.50	.054	.183	.032	.138	.109	.439	Potasan®
O,O-Dimethyl O-4-methyl umbelliferone thiophosphate	.087	.347	.042	.733	.075	1.099	.069	.310	Methyl potasan
O-Ethyl O-p-nitrophenyl thionobenzenephosphonate	.096	.221	.152	.440	.021	1.12	.001	.030	EPN®
O-Methyl O-p-nitrophenyl thionobenzenephosphonate	.082	.287	.336	.683	.071	1.359	.001	.056	MPN
O,O-Diethyl O-2-chloro-4-nitrophenyl thiophosphate	.195	1.645	.058	.293	.168	1.84	.087	1.323	
O,O-Dimethyl O-2-chloro-4-nitrophenyl thiophosphate	.181	.688	.035	.263	.546	6.942	.006	5.907	
O,O-Diethyl S-carbamylethyl dithiophosphate	.600	2.842	.003	.064	.308	.950	5.589	21.67	
O,O-Dimethyl S-carbamylethyl dithiophosphate	.170	.672	.176	.747	.254	1.10	2.72	12.8	
O-Ethyl O-o-nitrophenyl thionobenzenephosphonate	1.505	6.83	.274	.66	.031	.108	.048	.216	
O-Methyl O-o-nitrophenyl thionobenzenephosphonate	.432	.705	.412	1.07	.104	.334	1.423	6.438	
O,O-Diethyl O-ethylmercaptoethyl thiophosphate	3.919	15.92	.003	.036	.013	.051	2.56	99.07	Systox®
O,O-Dimethyl O-ethylmercaptoethyl thiophosphate	3.09	11.48	.017	.074	.037	.138	4.53	23.32	Meta-Systox®
O,O-Diethyl S-mercaptoacetylurea dithiophosphate	4.90	92.13	.009	.031	.022	.154	4.61	59.0	
O,O-Dimethyl S-mercaptoacetylurea dithiophosphate	1.53	10.73	.012	.054	.165	.464	.319	.823	
Tetraethyl dithiopyrophosphate	3.07	7.97	.340	2.14	.22	2.91	.81	6.61	
Tetramethyl dithiopyrophosphate	12.8	52.9	1.395	17.31	.605	2.12	1.32	9.33	

Compound (Applied as Sprays)	Septanychus								Aphis gossypii							
	Lbs/Acre For		Lbs/Acre	% Kill on Residues Of Age (Days)					Lbs/Acre For		Lbs/Acre	% Kill On Residues Of Age (Days)				
	50% Kill	90% Kill		1	3	7	10	14	50% Kill	90% Kill		1	3	7	10	14
TEPP	0.003	0.005	0.05	100	97	62	0	0	0.006	0.045	0.03	97	90	58	0	0
Parathion	.008	.015	.06	99	100	96	67	49	.016	.090	.06	95	96	95	85	26
Potasan®	.012	.022	.06	84	98	91	95	98	.027	1.58	.2	69	80	14	25	41
Sulfatep	.022	.041	.06	96	97	27	33	53	.195	.684	.2	48	15	38	0	0
OMPA	.139	.321	.5	93	100	90	100	100	.031	.062	1.0	98	100	100	100	100

(2) Results obtained using some organic phosphorus compounds in fly baits: 1915

Compound	Concentration (%)	% Killed Or Down (Laboratory Tests) After			Control In Field
		30 Min	1 Hr	24 Hrs	
Dipterex®	0.1	54.5	56.5	100	Excellent
Diazinon	1.0	23	36	90	Excellent
Malathion®	1.0	43	56	93	Excellent
Metacide	1.0	23	23	100	–
NPD	1.0	36	40	90	–
Parathion	1.0	13	13	90	–
TEPP	0.5	53	56	100	–

(3) Toxicity for various insects of organic phosphorus compounds; as dusts in pyrophyllite; by direct contact action: 2076

Compound	Concentration (%)	Lbs/Age	% Mortality After 24 Hrs For				
			Melanoplus differentialis	Psallus seriatus	Anasa tristis	Aphis gossypii	Septanychus
Parathion	1	10	—	—	—	94.0	99.4
	2	6	62.2	—	—	—	—
	2	8	98.5	98.4	—	—	—
	5	25	—	—	59.4	—	—
O,O-Diisopropyl O-p-nitrophenyl thiophosphate	1	10	—	—	—	30.8	21.7
	2	6	9.4	—	—	—	—
	2	8	14.1	65.0	—	—	—
	5	10	—	—	—	—	29.2
	5	25	—	—	0.0	—	—
O,O-Diethyl O-2-chloro-4-nitrophenyl thiophosphate	1	10	—	—	—	95.2	99.7
	2	6	22.5	—	—	—	—
	2	8	0.0	96.5	—	—	—
	5	25	—	—	74.5	—	—
S-tert.-Butylmercaptoethyl O,O-bis-(2-chloroethyl) dithiophosphate	1	10	—	—	—	98.3	76.3
	2	6	14.7	—	—	—	—
	2	8	22.8	97.0	—	—	—
	5	25	—	—	12.5	—	—
S-Carbamylmethyl diethyl dithiophosphate	1	10	—	—	—	89.0	86.3
	2	6	30	—	—	—	--
	2	8	21.8	68.9	—	—	—
	5	25	—	—	19.8	—	—
S-Carbamyl O,O-dimethyl dithiophosphate	1	10	—	—	—	53.5	50.5
	2	6	12.1	—	—	—	—
	2	8	30	51.5	—	—	—
	5	25	—	—	1.1	—	—
S-Mercaptoacetylurea O,O-diethyl dithiophosphate	1	10	—	—	—	80.7	87.2
	2	6	23.8	—	—	—	—
	2	8	10.5	72.2	—	—	—
	5	25	—	—	0.0	—	—
S-Mercaptoacetylurea O,O-dimethyl dithiophosphate	1	10	—	—	—	78.6	23.0
	2	6	26.0	—	—	—	—
	2	8	0.0	62.3	—	—	—
	5	25	—	—	4.1	—	—

(4) Toxicity of certain organic phosphorus compounds as stomach poisons: 2076

Compound	Concentration (%)	Lbs/Acre	% Mortality* Of		As Dusts Vs. Anthonomus grandis	
			Melanoplus differentialis	Anthonomus grandis	LD₅₀ (Lbs/Acre)	Regression
Parathion	2	12	53.6	—	0.1	2.8
"	5	12	100	97.9	—	—
O,O-Diisopropyl O-p-nitrophenyl thiophosphate	2	12	11.7	—	—	—
	5	12	0.0	11.4	—	—
	10	12	--	11.8	—	—
O,O-Bis-(2-chloroethyl)S-tert.-butylmercaptomethyl dithiophosphate	2	12	40.0	—	0.2	2.8
	5	12	0.0	26.1	—	—
	10	12	—	0.0	—	—
O,O-Diethyl O-2-chloro-4-nitrophenyl thiophosphate	2	12	0.0	—	0.3	1.8
	5	12	0.0	14.6	—	—
	10	12	—	29.4	—	—
O,O-Diethyl S-carbamylmethyl dithiophosphate	2	12	8.7	—	0.6	1.5
	5	12	1.8	15.0	—	—
	10	12	—	23.5	—	—
O,O-Dimethyl S-carbamyl dithiophosphate	2	12	44.0	—	0.4	3.9
	5	12	0.0	7.1	—	—
	10	12	—	0.0	—	—
O,O-Diethyl S-mercaptoacetylurea dithiophosphate	2	12	0.0	—	0.3	0.8
	5	12	33.3	4.7	—	—
	10	12	—	0.0	—	—
O,O-Dimethyl S-mercaptoacetylurea dithiophosphate	2	12	32.7	—	0.3	2.3
	5	12	11.1	4.4	—	—
	10	12	—	7.1	—	—
Toxaphene + Sulfur	20-40	12	—	95.7	—	—

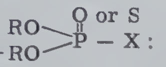
*Note: Apparent reduction in mortality at high concentrations is accounted for by repellent action at such concentrations.

(5) Action of some organic phosphorus compounds on lice of livestock: 2862

Insecticide	As spot Treatment Vs. Haematopinus eurysternus *% Mortality 24, 48 hrs. At Conc. (%) Shown									As Dips Vs. Bovicola caprae, B. limbatus **% Mortality 24, 48 hrs At Conc. (%) Shown						
	1.0	.5	.25	.2	.1	.05	.01	.005	.002	.25	.1	.05	.025	.01	.005	.002
Malathion	—	100_2	—	—	—	100_1	—	—	—	100_0	100_0	100_0	100_0	—	—	—
Parathion	—	—	—	—	—	100_3	100_3	25_0	—	—	—	—	—	—	—	—
Chlorthion®	—	—	100_1	—	—	—	—	—	—	—	—	—	—	—	—	100_0
Dipterex®	—	—	100_1	—	100_0	—	—	—	—	—	100_+	100_+	100_+	100_+	—	100_+
Bayer 21/199	—	—	100_2	100_2	100_1	—	—	—	—	—	—	—	—	—	—	100_0
Diazinon	—	—	100_2	—	100_2	100_1	95_1	25_1	5_1	—	—	100_0	100_0	—	100_+	—
Pirazinon	—	—	100_3	—	—	—	—	—	—	—	—	—	—	—	—	—
EPN®	—	—	—	—	—	100_1	100_1	100_1	25_0	—	—	—	—	—	—	100_0
NPD	—	—	—	—	—	100_1	—	—	—	—	—	—	—	—	—	25_+
Bayer 21/200																

*Subscript = weeks effective **Subscript 0 = no reinfestation after 4 weeks; + = light reinfestation after 4 weeks.

d) SOME GENERALIZATIONS ON STRUCTURE AND TOXICITY IN ORGANIC PHOSPHORUS COMPOUNDS:

(1) Variation of alkyl groups (R) in  $\begin{matrix}RO\\RO\end{matrix}\!>\!\overset{\text{O or S}}{\overset{\|}{P}} - X$: [522,587,1791,2069]

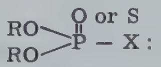
(a) In toxicity for laboratory animals the tendency is $(CH_3)_2 < (C_2H_5)_2 < (isoC_3H_7)_2$ with $(n\text{-}C_4H_9)_2$ and $(\text{iso-amyl})_2$ of low toxicity as shown by dialkyl fluorophosphates. ID_{50} values for horse serum ChE inhibition followed a similar trend. However, dicyclohexyl, di-sec.-butyl, di-1,3-dimethyl-n-butyl fluorophosphates tend to be very toxic.

(b) In pyrophosphates, tetra-C_2H_5 is associated with maximal toxicity for mice, being twice as toxic as 3104
tetra-CH_3, 16 times as toxic as tetra-iso-C_3H_7 (intraperitoneally). Ability to inhibit serum ChE *in* 3105
vitro follows the same trend. 3106
2769,3090

(c) Among the parathion and para-oxon series, $(C_2H_5)_2$ is >toxic than $(CH_3)_2$ by 2-3 times (ip to 1475
mouse, or to rat, topically to *Musca*); for *Apis mellifera*, methyl parathion and methyl para-oxon 2244
are more toxic by 2 times than the $(C_2H_5)_2$ homologues. $(n\text{-}C_3H_7)_2$ and $(iso\text{-}C_3H_7)_2$ are less toxic
for insects. Trend of ability to inhibit horse serum and bee brain ChE follows toxicity.

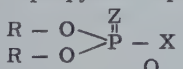
(d) The $(CH_3)_2$ homologues of the following tend to be less toxic for mammals than the diethyl 1709,2773
compounds (which are the ones named): Malathion, Systox®. Insecticidal activity follows the 2768,1543
same trend but, relatively, remains much higher than mammalian toxicity; thus, $(CH_3)_2$ esters 29,395
may be eminently practical insecticides, for instance methyl parathion, Meta-Systox®, 3323,2119
American Cyanamid 4124, Chlorthion®.

(e) Replacement of one or both alkoxy group(s) by aryloxy group(s) yields marked decrease in toxicity 1786
for insects. Substitution of a phenyl group for one alkoxy (see EPN®) yields in the case of EPN®
high insect toxicity.

(2) Variation in group (X) of  $\begin{matrix}RO\\RO\end{matrix}\!>\!\overset{\text{O or S}}{\overset{\|}{P}} - X$:

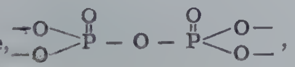
(a) Esters of relatively strong acids tend to be of high toxicity, and those of weak acids are relatively 1785,29
non-toxic, for instance triethyl- and diethylphenyl- phosphate are non-toxic; TEPP, diethyl 2244,31
fluorophosphate, diethyl acetyl phosphate, diethyl benzoyl phosphate are very toxic. (See the 2069,2150
preceding tabulation of the comparative toxicities of the diethyl aryl phosphates.) 391,1677,3212

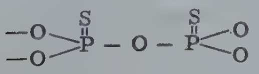
(b) Dithiophosphoric acid esters: Some (such as O,O-diethyl S-2-ethyl mercaptomethyl dithio- 2231
phosphate and the S-2-isopropyl mercaptomethyl analogue) are more toxic than parathion for 1656
mammals by 5-10 times as well as being effective insecticides by contact and "systemic
action." O,O-Dimethyl S-(2-oxoureidoethyl- and O,O-dimethyl S-carbamylmethyl- dithiophosphates show high contact toxicity for insects as well as systemic activity. Malathion (O,O-dimethyl S-(1,2-dicarboethoxyethyl) dithiophosphate) is not only effectively insecticidal and acaricidal, but has relatively low mammalian toxicity, the latter being less than one thousandth that of the S-(2-isopropylmercaptomethyl)-analogue.

(3) Variations at (Z) in  $\begin{matrix}R-O\\R-O\end{matrix}\!>\!\overset{Z}{\overset{\|}{P}} - X$ (phosphoryl vs. thiophosphoryl, etc.)

(a) These variations comprise: $>\overset{O}{\overset{\|}{P}}-$, $>\overset{S}{\overset{\|}{P}}-$, $>\overset{Se}{\overset{\|}{P}}-$; namely: thiophosphate, thionophosphate, 2244,3365,2769
selenophosphate. 2891,326

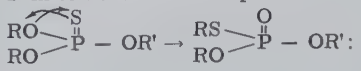
(b) Thionophosphates tend to be decidedly less toxic than thiophosphates both for mammals and insects. Para-oxon ($>\overset{O}{\overset{\|}{P}}-$) is more toxic than parathion ($>\overset{S}{\overset{\|}{P}}-$) for mouse (ip), rat (or), *Musca*, *Periplaneta* (topical; injection), *Apis* (topical) being, however, less toxic for *Sitophilus granarius* (contact). Methyl-para-oxon is likewise more toxic than methyl- parathion for mouse, rat, *Apis* but is ca. "equitoxic" to methyl parathion for *Musca*. Methyl-para-oxon is likewise more effective for *Sitophilus granarius* than is parathion. In the case of contact toxicity for *Sitophilus*, replacement of $>\overset{S}{\overset{\|}{P}}-$ by $>\overset{O}{\overset{\|}{P}}-$, or alteration in the size of groups on the central P atom, yields decline of toxic action.

(c) Pyrophosphate,  $\begin{matrix}-O\\-O\end{matrix}\!>\!\overset{O}{\overset{\|}{P}} - O - \overset{O}{\overset{\|}{P}}\!<\!\begin{matrix}O-\\O-\end{matrix}$, (as in TEPP) is more toxic than dithionopyrophosphate 2244

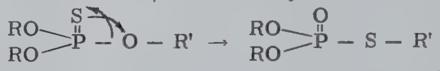
 $\begin{matrix}-O\\-O\end{matrix}\!>\!\overset{S}{\overset{\|}{P}} - O - \overset{S}{\overset{\|}{P}}\!<\!\begin{matrix}O\\O\end{matrix}$ (as in Sulfatep) for mouse (ip), *Apis* and aphids. 2773

(d) In general, replacement of $>\overset{O}{\overset{\|}{P}}-$ by $>\overset{S}{\overset{\|}{P}}-$ yields decline in insect and mammalian toxicity. There are indications that thionophosphate must become thiophosphate by metabolic action to yield toxic activity, thus, $>\overset{O}{\overset{\|}{P}}-$ yields more rapid action than $>\overset{S}{\overset{\|}{P}}-$, e.g. para-oxon and parathion vs. Musca. Thiophosphates are more water-soluble by far than thionophosphates and undergo more rapid hydrolysis in alkaline media. Stability favors the thionophosphates as practical insecticides. 2248

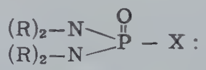
(e) With Se at (Z) (as $>\overset{Se}{\overset{\|}{P}}-$) there is high toxicity for mammals; the selenium-analogue of TEPP is about equal to TEPP in toxic action vs. aphids.

(4) Isomerization: 
$(RO)_2\overset{S}{\overset{\|}{P}}-OR' \rightarrow \frac{RS}{RO}>\overset{O}{\overset{\|}{P}}-OR'$:

(a) Parathion and similar compounds undergo isomerization by heat: Parathion (O,O-Diethyl (O-p-nitro- 2244
phenyl thionophosphate) $\xrightarrow{heat}$ O,S-diethyl O-p-nitrophenyl thiophosphate, with the following con- 3365
sequences: Toxicity to mouse (sc) unchanged; to rat (or) decline by 10 times; to Musca (topical) 2248
and Sitophilus granaruis (contact) marked decline. Anti-ChE action in vitro is enhanced over that 1475
of parathion, but still greatly inferior to para-oxon activity. The isomerization Methyl parathion 2243
(O,O-dimethyl O-p-nitrophenyl thionophosphate) $\xrightarrow{heat}$ O,S-dimethyl O-p-nitrophenyl thiophosphate 218
yields changes in mammalian and insect toxicity and anti-ChE activity parallel to the preceding. 32


$(RO)_2\overset{S}{\overset{\|}{P}}-O-R' \rightarrow (RO)_2\overset{O}{\overset{\|}{P}}-S-R'$

(b) Parathion may undergo isomerization according to the type change shown above [as may O,O- 205
diethyl O-2-ethylmercaptoethyl thionophosphate (Systox® thiono-isomer)] to yield the thiol-isomer, 1111
O,O-diethyl S-2-ethylmercaptoethyl thiophosphate. Methyl parathion undergoes a comparable iso- 1475
merization. Parathion-S-phenyl-isomer is insecticidal. The S-phenyl isomer of parathion (like 2651
that of methyl parathion) has a mammalian toxicity decidedly enhanced over that of the O-phenyl 2236
isomer. Anti-ChE activity of the S-phenyl isomers of parathion and methyl parathion is greater 2773
than that of para-oxon and methyl para-oxon. The toxicity for the mouse of Systox® thiol-isomer 30
is much more than that of the thiono-isomer. Likewise, thiol-Systox® is more effective as a 442
systemic insecticide.

(5) Alkyl groups of amidohalogenophosphates (pyrophosphoramides) 
$((R)_2-N)_2\overset{O}{\overset{\|}{P}}-X$:

(a) In toxicity to mammals among the bis-(di(x)amino) fluorophosphine oxides the trend is $[(CH_3)_2N)_2] < [(C_4H_9)_2N]_2 < [(dicyclohexyl)_2N]_2$. 1467

(b) Among the halogenophosphates bis-(dimethylamino) fluorophosphine oxide (BFPO) is low in horse serum ChE inhibitory action. Bis-(monoisopropylamino) fluorophosphine oxide (Isopestox®) potently inhibits ChE. In toxicity for mammals, nevertheless, BFPO is far more toxic than Isopestox®. 141

(c) OMPA (Schradan) is a weak in vitro ChE inhibitor (27% inhibition at 1×10^{-2}M) while its analogue, tetraisopropyl pyrophosphoramide, yields 50% ChE inhibition at 6×10^{-6}M. 141

e) QUANTITATIVE SUMMARY OF TOXICITY AND ANTI-CHOLINE ESTERASE ACTIVITY OF CERTAIN ORGANIC PHOSPHORUS COMPOUNDS FOR HIGHER ANIMALS:

I) Halogenophosphates

(a) Diethyl fluorophosphate: Mouse LC_{50}, inhalation = 0.5 mg/1 (78 ppm) 10 min. exposure. 2834

(b) Di-isopropyl fluorophosphate (DFP)

Animal	LD_{50} (mg/k)					
	or	ct	sc	im	ip	iv
Mouse	36.8	72	4.67	—	—	—
Rat	♀ 7.7 ♂13.5	—	3	2	—	—
Rabbit	4.0-9.8	117	1	0.75	1	0.34
Cat	—	—	—	—	—	1.63±.03
Dog	—	—	3	—	—	3.43±.62
Monkey	—	—	—	—	—	0.25-0.3
Goat	—	—	1	—	—	0.8

(c) ID_{50} Horse serum ChE In Vitro 2069

Dimethyl fluorophosphate	1×10^{-7} M
Diethyl "	8×10^{-9} M
Di-isopropyl "	1.3×10^{-9} M
Di-n-propyl "	5.5×10^{-9} M
Di-sec.-butyl "	2×10^{-9} M
Diphenyl	6.3×10^{-8} M

II) Amidohalogenophosphates; Pyrophosphoramides:

II) Amidohalogenophosphates; Pyrophosphoramides: [129,2120,1467,2651,2410,861,29]

(a)

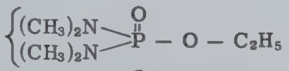
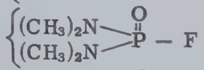
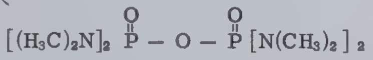
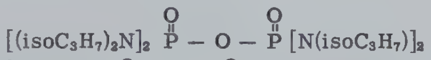
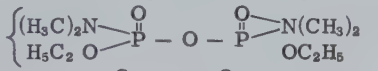
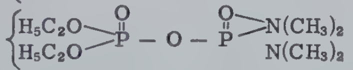
	LD$_{50}$ (mg/k)					
	BFPO*				Isopestox® **	
	or	sc	ip	iv	or	ip
Rat	7.5	—	5.0	—	—	25-50
Mouse	—	1.0	1.4; 5.0	—	—	—
Guinea Pig	—	—	2.5	—	80-100	—
Dog	—	—	—	5-10	—	—
Rabbit	—	—	—	—	80-100	—

	ID$_{50}$	ID$_{50}$
Horse plasma ChE	4.9 x 10^{-4} M	3.6 x 10^{-8} M
Rat Brain ChE	4 x 10^{-5} (in vitro)	—
True ChE	—	3.8 x 10^{-8} M
Pseudo ChE	—	1.5 x 10^{-4} M

*Bis-(dimethylamino) fluorophosphine oxide.
**Bis-(monoisopropylamino) fluorophosphine oxide.

(b) Mouse LD$_{50}$ sc for bis- di C_2H_5-, dibutyl-, dicyclohexyl- amino fluorophosphine oxides = 160, 16, 9.

(c) [1790,497,861,141]

Compound	Formula	Rat LD$_{50}$,ip (mg/k)	ID$_{50}$ ChE in vitro
Ethyl di(dimethylamido) phosphate	 $\left\{\begin{matrix}(CH_3)_2N\\(CH_3)_2N\end{matrix}\right> \overset{O}{\overset{\|}{P}} - O - C_2H_5$	>1500	> 1 x 10^{-2} M
Bis (dimethylamido) phosphorofluoridate (BFPO)	 $\left\{\begin{matrix}(CH_3)_2N\\(CH_3)_2N\end{matrix}\right> \overset{O}{\overset{\|}{P}} - F$	5	4 x 10^{-5} M
Octamethyl pyrophosphoramide (OMPA)	 $[(H_3C)_2N]_2\ \overset{O}{\overset{\|}{P}} - O - \overset{O}{\overset{\|}{P}}[N(CH_3)_2]_2$	8	≫1 x 10^{-2} M* Human red cell → 4.5 x 10^{-2} M Rat brain → 1.5 x 10^{-1} M
Tetraisopropyl pyrophosphoramide	 $[(isoC_3H_7)_2N]_2\ \overset{O}{\overset{\|}{P}} - O - \overset{O}{\overset{\|}{P}}[N(isoC_3H_7)]_2$	—	6 x 10^{-6} M
Diethyl di(dimethylamido) pyrophosphate	 $\left\{\begin{matrix}(H_3C)_2N\\H_5C_2\ O\end{matrix}\right> \overset{O}{\overset{\|}{P}} - O - \overset{O}{\overset{\|}{P}} \left<\begin{matrix}N(CH_3)_2\\OC_2H_5\end{matrix}\right.$	11.5	4.7 x 10^{-7} M
Diethyl di(dimethylamido) pyrophosphate	 $\left\{\begin{matrix}H_5C_2O\\H_5C_2O\end{matrix}\right> \overset{O}{\overset{\|}{P}} - O - \overset{O}{\overset{\|}{P}} \left<\begin{matrix}N(CH_3)_2\\N(CH_3)_2\end{matrix}\right.$	2.7	2.8 x 10^{-7} M

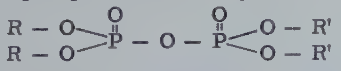
*At 1 x 10^{-2} M only 27% inhibition of horse plasma ChE could be obtained.

(d) 2773,1057 860,1951 861,2653 129,1952

	Octamethyl pyrophosphoramide (OMPA) LD$_{50}$ (mg/k)				
	or	sc	ct	ip	iv
Mouse	30	1.5-7.0 (LD)	—	8;17	—
Rat	♂13.5 ♀35.5	18(LD)	—	8-8.5	—
Guinea Pig	15.0	—	—	10.0	—
Rabbit	25	—	ca780	—	—
Dog	—	—	—	—	5-10

III) Pyrophosphates; Dithionopyrophosphates:

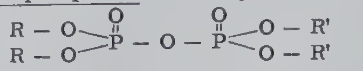
(a) Alkyl pyrophosphates: Toxicity for the mouse; anti-ChE activity:


$$\left.\begin{matrix}R-O\\R-O\end{matrix}\right> \overset{O}{\overset{\|}{P}} - O - \overset{O}{\overset{\|}{P}} \left<\begin{matrix}O-R'\\O-R'\end{matrix}\right.$$

[861,2775,3104,3105,89,1057,2081,1284, 326,859]

R	R'	ID$_{50}$ ChE For		LD$_{50}$ (mg/k) For					
				Mouse			Rat		
		Man (serum)	Mouse (brain)	or	sc	ip	or	sc	ip
CH_3	CH_3	2 x 10^{-6} M	1.8 x 10^{-8}	—	—	—	—	—	1.9;1.7
CH_3	C_2H_5	—	8 x 10^{-9}	—	—	—	—	—	1.4;1.1
CH_3	n-C_3H_7	—	—	—	—	—	—	—	1.9
CH_3	iso-C_3H_7	—	2 x 10^{-7}	—	—	—	—	—	3.0;2.5
C_2H_5*	C_2H_5*	8.6 x 10^{-10}	4 x 10^{-9}	7.0	0.9	0.82;0.85	♀1.2♂2.0	0.7	0.65;0.85
C_2H_5	n-C_3H_7	—	—	—	—	—	—	—	1.6
C_2H_5	iso-C_3H_7	—	—	—	—	—	—	—	2.8
C_2H_5	n-C_4H_9	—	—	—	—	—	—	—	2.1
n-C_3H_7	n-C_3H_7	2.8 x 10^{-8}	—	—	—	—	—	—	9.5
n-C_3H_7	iso-C_3H_7	—	—	—	—	—	—	—	17

(a) Alkyl pyrophosphates: Toxicity for the mouse; anti-ChE activity:

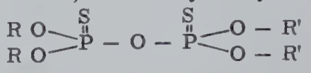


$(R-O)_2P(=O)-O-P(=O)(O-R')_2$ [861,2775,3104,3105,89,1057,2081,1284, 326,859]

R	R'	ID$_{50}$ ChE For		LD$_{50}$ (mg/k) For					
		Man (serum)	Mouse (brain)	Mouse			Rat		
				or	sc	ip	or	sc	ip
iso-C_3H_7	iso C_3H_7	—	1.4 x 10^{-6}	—	—	—	—	—	13.3;16.0
iso-C_3H_7	n-C_4H_9	—	—	—	—	—	—	—	8.4
n-C_4H_9	n-C_4H_9	1.2 x 10^{-9}	—	—	—	—	—	—	14.2

*Other toxicity and anti-ChE activity data for TEPP: Guinea Pig, or, 2.3; rabbit, ct, 5, 2.0-2.5; cat, sc 2.5-3.0. ID$_{50}$ in vitro for: Human plasma ChE 5 x 10^{-9}; human erythrocyte ChE 3.5 x 10^{-8}, human brain ChE 3.2 x 10^{-8}.

(b) Alkyl dithionopyrophosphates

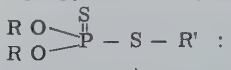


$(RO)_2P(=S)-O-P(=S)(O-R')_2$:

R	R'	LD$_{50}$ (mg/k) For		
		Mouse	Rat	
		sc	or	ip
1* C_2H_5	C_2H_5 (Sulfatep)	8	5	—
2** n-C_3H_7	n-C_3H_7 (NPD)	—	1450	1100

*Tetraethyl dithionopyrophosphate **Tetra-n-propyl dithionopyrophosphate.

IV) Dithiophosphates (Phosphorodithioates):



$(RO)_2P(=S)-S-R'$: [2802,2231,353,1092,1308,1458,1123,854,3188 1085,2582,1915,2862,473,775,1660]

(a) Malathion (O,O-dimethyl S-(1,2-dicarboethoxyethyl) dithiophosphate) is the most important of this group of organic phosphorus compounds in present use as an insecticide. Three others have been tested and found to have contact, and/or "systemic" insecticidal or acaricidal action namely, O,O-diethyl S-2-isopropyl mercaptomethyl dithiophosphate (TM 12008), O,O-diethyl S-propyl mercaptomethyl dithiophosphate (TM 12009), O,O-diisopropyl S-isopropyl mercaptomethyl dithiophosphate (TM 12013). O,O-dimethyl) S-(2-oxoureidoethyl) dithiophosphate and O,O-dimethyl S-carbamylmethyl dithiophosphate are described as effective contact and "systemic" agents against insects. Malathion is outstanding by virtue of its relatively low toxicity for mammals, having less than 1/1000th the toxicity of TM 12008.

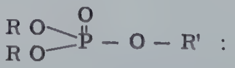
(b) Toxicity of malathion varies greatly with the vehicle or solvent used, and with the degree of purity; the values which follow must be considered with this in mind. Some sexual differences in susceptibility are also suggested. 1577,1331 854,1216 2231,1461

	Malathion LD$_{50}$ (mg/k)			
	or	ct	ip	iv
Mouse	720,885,2700,3300	—	—	—
Rat	390,480,940,1500,4700	>4000	750	ca50
Guinea Pig	570	—	—	—
Cow	560	—	—	—
Calf (3 wks old)	80	—	—	—
Chicken	>850	—	—	—

	ID$_{50}$ ChE, in vivo; in vitro
Rat Serum ChE in vitro	8 x 10^{-3} M
Rat Erythrocyte ChE in vitro	2 x 10^{-5} M
Rat ChE in vivo	1 x 10^{-1} M
Mouse Brain ChE in vitro	150 x 10^{-6} M

	ID$_{50}$, Rat ChE in vivo, Comparative	LD$_{50}$, ip, (mg/k)
Malathion	1 x 10^{-1} M	750
Parathion	1.2 x 10^{-6} M	5.5
Metacide®	1 x 10^{-9} M	3.5
Potasan®	5 x 10^{-5} M	15.0
Systox®	5 x 10^{-7} M	3.0

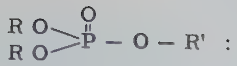
V) Orthophosphates:



$(RO)_2P(=O)-O-R'$:

(a) Comparative toxicity of some insecticidal orthophosphates for higher animals: [1121,1837,2140,1475,857,2231]

Toxicant	LD$_{50}$ (Unless Otherwise Noted) (mg/k) For							
	Frog	Mouse		Rat			Rabbit	
	sc	or	sc	or	ct	ip	or	ct
Para-oxon	30*	—	2*	3.0* 3.5	—	—	—	5
O,O-Dimethyl O-2,2-dichlorovinyl phosphate	—	—	—	80 ♂ 56 ♀	107♂ 75♀	—	—	—

V) Orthophosphates: 

$(RO)_2P(=O){-}O{-}R'$:

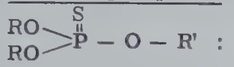
(a) Comparative toxicity of some insecticidal orthophosphates for higher animals: [1121,1837,2140,1475,857,2231]

Toxicant	LD50 (Unless Otherwise Noted) (mg/k) For							
	Frog	Mouse		Rat			Rabbit	
	sc	or	sc	or	ct	ip	or	ct
O,O-Diethyl O-2-chlorovinyl phosphate	—	32.9♂ 18.0♀	—	10.0♂ 10.5♀	—	9.0	3.4♂	17.6♂
O,O-Dimethyl O-1-carbomethoxy-1-propen-2-yl phosphate	—	7.8♂ 4.3♀	—	6.8♂ 6.0♀	—	1.5♀	—	33.8
Pyrazoxon	—	4.0	—	—	—	—	—	—

*MLD

	ID50 ChE	(In Vitro)	
Para-oxon (purified)	2.01×10^{-8} M	Sheep red cell ChE	31,713
"	4.2×10^{-7} M	True-ChE	29
"	1.4×10^{-7} M	Pseudo-ChE	29
O,O-Diethyl-O-2-chlorovinyl phosphate	1.7×10^{-5} M	Human erythrocyte ChE	1837
O,O-Dimethyl O-1 carbomethoxy-1-propen-2-yl phosphate	2.3×10^{-6} M	" " "	1837

VI) Orthothiophosphates (phosphonothioates, thionophosphates, phosphorothionates, phosphorothioates) [1475,3148,1057,861,746,3148,57,1462,857,30,1278,863,1653,2231,368,713,3204, 2120,2803,1121,369,1123,854,1384,2651,188,2768,1951,2247,2773,32]



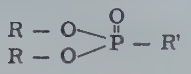
$(RO)_2P(=S){-}O{-}R'$:

Insecticide	LD50 (mg/k) For											
	Frog	Mouse			Rat			Guinea Pig	Rabbit		Cat	Dog
	sc	or	sc	ip	or	ip	iv	or	or	ct	ip	ip
Parathion	200*	25	15-25	5.5	♀ 3.5, 3.0, 6, ♂ 12.5, 30, 15 4.4	♀ 4 ♂ 7	3**	32	—	870 420 40-50	3-5	12-20
Methyl parathion	—	100-200	50-100**		14-42	3.5	—	—	420**	300-400		
Chlorthion®	—	—	—	—	500;1500	750	—	—	—	—	—	—
Potasan®	—	98.5	—	—	♂ 42.0 ♀ 19.0	15.0	—	25.0	—	ca300	—	—
Diazinon	—	82;ca100	—	—	220-270 ca900;100-150	—	—	320mm³/k	130mm³/k	>4000	—	—
Pyrazothion	—	12	—	—	36	—	—	—	—	—	—	—
Experimental Cpd. 4124	—	1350;400***	—	—	1710;1310	—	—	—	—	—	—	—
Systox®	—	—	—	>20†;<2††	7.5† 1.5†† 9-10;6-12	3	—	—	—	24	—	—

* = MLD; ** = LD ***Compare with 31.5 for diethyl analogue; †= thiono-isomer; ††= thiol-isomer.

Insecticide	Enzyme Preparation (ChE)	ID50 ChE in vitro; in vivo
Parathion*	Rat brain	1.2×10^{-6} M (in vivo)
"	Human erythrocyte	1.2×10^{-5} M (")
"	Human plasma	1.5×10^{-6} M (")
Methyl parathion (Metacide)	Rat ChE	1×10^{-4} M (")
Chlorthion®	Rat brain	5×10^{-6} M (in vitro)
Potasan®	Rat ChE	5×10^{-9} M (in vivo)
Diazinon	Rat plasma	1×10^{-5} (in vitro)
"	Rat erythrocyte	1×10^{-7} (")
"	Rat brain	1×10^{-6} (")
Systox®	Human plasma	8×10^{-6} (")
"	Rat ChE	5×10^{-7} (in vivo)
" thiono-isomer	Human serum	1×10^{-5} (in vitro)
" thiol-isomer	Human serum	3×10^{-6} (")
"	Rat plasma	2.4×10^{-6} (")
"	Rat brain	4×10^{-6} (")

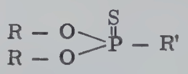
*Parathion, in the pure or highly purified state, is a weak in vitro inhibitor of ChE. Nearly all of the in vitro 32,713
activity variously reported for parathion is attributed to impurities which are potent in vitro ChE inhibitors.

VI) Phosphonates; 

$(R{-}O)_2P(=O){-}R'$:

Insecticide	LD50 (mg/k) For				
	Mouse	Rat		Guinea Pig	Rabbit
	or	or	ip	or	ct
Dipterex® (O,O-Dimethyl-2,2,2-trichloro-1-hydroxyethyl phosphonate)	500	450;500	225	300	5000 (LD)

ID50 Rat Brain ChE in vitro
2×10^{-6} M

VII) Thionophosphonates (phosphonothioates);  $\frac{R-O}{R-O}{>}\overset{S}{\overset{\|}{P}}-R'$: [1057,874,1553,797,2231]

Insecticide	Mouse		Rat		Guinea Pig		Rabbit	
	or	ip	or	ip	or	ip	ct	ip
EPN®	45.5	48	40(♂)	108(♂)	79.4(♂♀)	20-30(♂♀) LD_{100}	50(♂)LD_{100}	80(♂)LD_{100}
(Ethyl-p-nitrophenyl benzenethionophosphonate)			12(♀)	26(♀)			150(♀)LD_{100}	20(♀)LD_{100}
			*42(♂)	64(♂)				
			*14(♀)	24(♀)				
			7;8,13(♀)					
			28;33(♂)					

*Crystalline EPN.

(a) The in vitro anti-choline esterase activity which has been attributed to EPN® is apparently due to impurities. Freshly purified, recrystallized EPN® lacks choline esterase inhibitory activity in vitro. The toxicity for Guinea pig of samples of the highest purity and samples of lesser purity is virtually the same by acute or oral dosage. It is postulated that a rapid conversion of EPN® in vivo yields a substance highly inhibitory of choline esterase, the inhibition being of the second order and irreversible.

VIII) Miscellaneous:

(a) Diethyl dithiocarbamic anhydride of O,O-di-isopropyl thionophosphoric acid (diethyl dithiocarbamic phosphorodithioic anhydrosulfide, O,O-di-isopropyl ester), Holcomb Compound 326:

LD_{50} (mg/k) For			
Mouse			Rat
or	ip	sc	or
290	220	295	320

(1) Tests with isolated strips of turtle heart and with rabbit intestine indicated no inhibition of acetylcholine esterase.

f) PHARMACOLOGICAL, PHARMACODYNAMIC, PHYSIOLOGICAL AND BIOCHEMICAL CONSIDERATIONS OF ORGANIC PHOSPHORUS COMPOUNDS IN HIGHER ANIMALS:

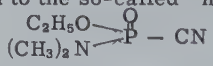
I) General Remarks: [713,1458,135,2342,1581,2231,353,3290,1843,276,978,2962,133,2646,852,851,1221]

(1) The organic phosphorus insecticides share in common 2 characteristics:

(a) Structurally, all possess the organic phosphate radical;

(b) Pharmacodynamically, they inhibit competitively and irreversibly the enzyme acetocholinesterase (= acetylcholine esterase) and other choline esterases.

(2) The biological action of these compounds centers on the process and system of neuro-effector transmission in which the humoral (neuro-hormonal) agent is acetylcholine and possibly close analogues such as butyrylcholine, benzoylcholine, etc.

(3) Organic phosphorus insecticides are related to the so-called "nerve gases," such as dimethylamidoethoxyphosphoryl cyanide ("Tabun")  $\frac{C_2H_5O}{(CH_3)_2N}{>}\overset{O}{\overset{\|}{P}}-CN$ which have intense activity as inhibitors of choline esterase(s).

(a) Vs. human erythrocyte ChE the ID_{50} of "Tabun" in vitro = 3.95×10^{-9} M, while the methyl and isopropyl analogues, respectively, have ID_{50}'s of 1.63×10^{-8} M and 1.27×10^{-9} M.

(4) The pharmacological effects derive from a pharmacodynamic action productive of imbalance in the essential enzyme system linked to the neuro-humoral mechanism in which acetylcholine serves as chemical mediator for autonomic ganglia, parasympathetic and somatic nerve systems (cholinergic systems) and, possibly the CNS (= central nervous system).

(a) Acetylcholine, the chemical mediator of transmission between nerve and effector, must be rapidly detoxified to prevent accumulation at (or in) the effectors with consequent signs of cholinergic intoxication.

(b) Choline esterase prevents acetylcholine accumulation as the enzyme which effects the hydrolysis of acetylcholine to yield acetic acid and choline which are inert in the neurohumoral sense.

(c) Inhibition of choline esterase yields excessive parasympathetic, somatic motor nerve and CNS stimulation effects.

II) Choline esterase, while it may not be the sole key to the toxic action of the organic phosphorus 1458,713,133
insecticides, appears to lie central to their action. Choline esterase is operationally recognized 2217,41,2150
by its action (in vitro) on acetyl- and other alkyl- cholines. 141,25,2341
13,2309,3001
353,2231

(1) Two operational entities satisfy the foregoing statement, namely:

(a) Acetocholine esterase (= "true," or "specific," choline esterase), present generally in erythrocytes and nerve tissue of most mammals and which functions in the hydrolysis of acetylcholine at the nerve ending.

(b) Pseudo-choline esterase (= "non-specific" choline esterase (s)) known, for example, from human serum, white matter of nerves, dog pancreas, etc., which in vitro hydrolyzes acetylcholine and various other esters. No specific function can be ascribed to this "entity" which is actually a "family" of substances. Some believe that in vivo it plays no part in acetylcholine hydrolysis. Others suggest a role in hydrolysis of acetycholine analogues important in various neuro-humoral functions. A wide variety of choline esterases appears to be universally distributed over the animal kingdom. Species differences among the esterases are marked and distribution in various taxonomic groups shows wide diversity.

(2) "True-" and "pseudo-" choline esterases reveal different kinetic properties and tissue distribution and may be differentially acted upon by diverse inhibitors, as well as showing a variety of specificities for choline esters, for example:

(a) "True" ChE hydrolyzes acetylcholine faster than it does other commonly known esters. It does not hydrolyze benzoylcholine but acts on acetyl-β-methylcholine.

(b) "Pseudo-" ChE (of human plasma) shows its maximum activity with butyrylcholine, hydrolyzes benzoylcholine but not acety-β-methylcholine.

(3) The following examples illustrate the confusing diversities among the "pseudo-" choline esterases and their distribution among animals:

(a) In plasma of some rabbits benzoyl ChE may be present with "True-" ChE, while sera of certain other rabbits contain (in significant amount) solely "True-" ChE.

(b) Among rabbit "pseudo-" choline esterases, butyrocholine esterase and benzoylcholine esterase 2473
have virtually identical substrate patterns with their horse-derived analogues but contrast with 1459
the latter by a low rate of acetylcholine splitting. Thus, the rabbit serum benzoylcholinesterase 1587
and intestine butyrocholine esterase appear to be distinct and specific entities. Rabbit liver contains yet another enzyme active for choline esters.

(c) Some sheep tissues are reported active with butyrylcholine as a substrate but not with benzoylcholine, thus differing from rat "pseudo-" choline esterase. 715

(d) An esterase of pig serum is reported active with acetylcholine as a substrate but inactive toward benzoyl- and acetyl-β-methylcholines (compare with human plasma ChE). 1980

(e) A chicken serum ChE is reported which splits acetyl-, benzoyl- and acety-β-methyl-choline but which (in its response to DFP) suggests a wholly "pseudo-" esterase. 892

(f) The ChE of rat heart appears identical with the pseudo ChE of the intestinal mucosa. Dog heart ChE resembles, but is not the same as, rat heart ChE. Goat heart ChE is reported to be "true-" ChE. In the horse, sympathetic ganglia and trigeminal ganglion possess "true-" ChE exclusively, while ciliary ganglion and post-ganglionic nerve contain both "true-" and "pseudo-" ChE. 713

(4) Choline esterase inhibitors likewise reveal specificity of action, for example: 141

(a) Iso-OMPA (N,N'-di-isopropyl phosphorodiamidic anhydride) is highly selective for "pseudo-" ChE which it inhibits competitively and irreversibly.

(b) Other inhibitors, for example 1,5-di-(p-N-allyl-N-methylamino) phenylpentan-3-one, act upon "true-" ChE reversibly and competitively.

(5) Summary: Choline esterase may be taken to refer to a "family" of enzymes which (as a whole) 713,139
hydrolyzes acetylcholine in vitro but the specificity of whose individual members toward other 1840,1841
choline esters is quite wide and whose roles in vivo (from the standpoint of these choline- 1842,176
ester specificities) remain obscure. 2416,2339

(a) Acetocholinesterase is certainly the enzyme at the nerve endings.

(b) As for the other choline esterases, the in vivo substrates and action are not yet elucidated.

(c) It is suggested that the cholinergic chemical mediation is in vivo not performed alone by acetycholine but that other related compounds play a part. Inference, then, would direct the so-called "pseudo-" esterases toward these other choline esters as substrates.

(d) The outstanding difference between "true-" and "pseudo-" ChE (as a generalization) is specificity respectively for acetates and butyrates.

III) Organic phosphorus insecticides as inhibitors of choline esterase(s): [28,24,31,306,1681,1419,1679,32]

(1) It is suggested that the organic phosphorus ChE inhibitors being esters may link themselves to the active center of choline esterase in the same manner as carboxylic esters. The inhibitor is then hydrolyzed, but the enzyme phosphate thus formed has its own stability toward hydrolysis which is dependent on the groups attached to the phosphorus atom. Potency reflects no high affinity for enzyme, but rather that one active center is made inactive by each reaction of an enzyme molecule and an inhibitor molecule.

(2) Proposed schema for ChE inhibition by organic phosphorus compounds:

(a) Reaction of these compounds with esterases appears to be in 1:1 molar ratio.

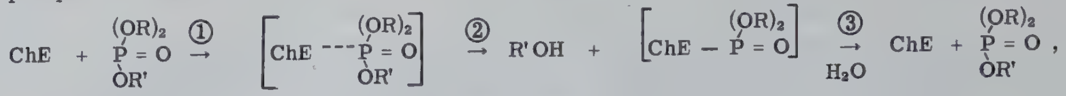
(b) General schema:

$$\underset{\text{(Enzyme)}}{E} + \underset{\text{(Inhibitor)}}{I} \longrightarrow \underset{\text{(Reversible Complex)}}{(EI)^R} \longrightarrow \underset{\substack{\text{(Irreversibly}\\ \text{Inhibited Enzyme)}}}{(E)^I} + \text{products,}$$

the inhibitor being hydrolyzed during the above process. Factors influencing may include: Length of the alkoxy-group of the inhibitor attached to P which governs "fit" of inhibitor and enzyme and, thus, ease of hydrolysis and inhibitory power.

(c) Two factors affect efficiency of an organic phosphate as inhibitor, namely: Stability toward hydrolysis and the group attached to the phosphorus atom.

(d) The inhibitory process is believed to comport a phosphorylation of the enzyme by the organic phosphorus inhibitor:

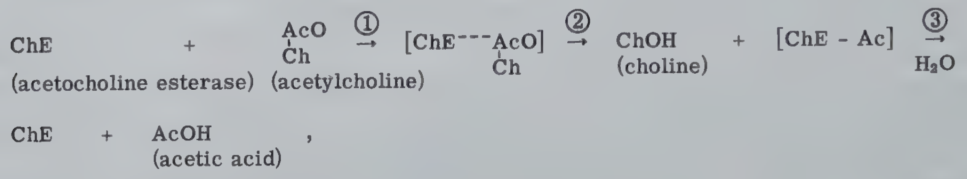


$$\mathrm{ChE} + \overset{(OR)_2}{\underset{OR'}{P}}=O \xrightarrow{\textcircled{1}} \left[\mathrm{ChE}\,{-}{-}{-}\overset{(OR)_2}{\underset{OR'}{P}}=O\right] \xrightarrow{\textcircled{2}} R'OH + \left[\mathrm{ChE} - \overset{(OR)_2}{P}=O\right] \xrightarrow[H_2O]{\textcircled{3}} \mathrm{ChE} + \overset{(OR)_2}{\underset{OR'}{P}}=O\,,$$

in which steps ① , ② comprise inhibition, step ③ reversal of inhibition, and in which step ③ is rate determining as it allows accumulation of inhibited enzyme from steps ① , ② .

(e) Some organic phosphorus compounds, for instance O,O-dimethyl O-p-nitrophenyl phosphate (methyl-para-oxon) yield a reaction which is readily reversible.

(f) The schema for the enzyme and inhibitor must be compared with the proposed schema for acetylcholine and acetylcholine esterase:



$$\underset{\text{(acetocholine esterase)}}{\mathrm{ChE}} + \underset{\text{(acetylcholine)}}{\underset{Ch}{AcO}} \xrightarrow{\textcircled{1}} [\mathrm{ChE}{-}{-}{-}\underset{Ch}{AcO}] \xrightarrow{\textcircled{2}} \underset{\text{(choline)}}{\mathrm{ChOH}} + [\mathrm{ChE} - Ac] \xrightarrow[H_2O]{\textcircled{3}}$$

$$\mathrm{ChE} + \underset{\text{(acetic acid)}}{\mathrm{AcOH}}\,,$$

in which step ③ must be fast, while the acylation of the enzyme (step ③) is rate determining.

IV) *General pharmacological and toxicological considerations*:

(1) The pharmacological effects of organic phosphorus insecticides are equivalent to an excessive accumulation of acetylcholine. The effects are produced by inhibition of choline esterase. In this connection the following comments are important: Nerve tissue contains acetocholine esterase, and conduction is abolished when 90% or more of the enzyme is blocked. Acetocholine esterase is universally present in nerves and muscle. In nerves it is localized at the neuronal surface and normal synaptic function depends on the presence of acetocholine esterase. Absence of the enzyme in the CNS leads to death. Inhibition and functional removal of the enzyme lead to various and complex organ and tissue failures. 2338 3322 2342 136

(2) Organic phosphorus insecticides are also known to inhibit other enzymes with esterase action, namely chymotrypsin, trypsin, citrus acetyl-esterase, liver esterase, milk lipase, tributyrinase, etc. 1684,1685 1682,1792 3250,2255

(3) In small doses, these compounds produce parasympathetic stimulation, yielding the following symptoms: Pupillary constriction with blurred vision, salivation; gastric motility with nausea, cramps; bronchial constriction with a sense of chest tightness. The parasympathetic activity signs may be blocked by atropine.

(4) On the choline esterase blocking activities of organic phosphorus compounds rests the rationale of their testing for use in *myasthenia gravis*, in place of such inhibitors as physostigmine, neostigmine or prostigmine. 851

I) *Symptomatology; signs of toxicity*: [851,852,678,1281,1283,714,237,749,59,89,1221]

(1) In general, the symptoms and signs of organic phosphorus insecticide poisoning resemble those elicited by di-isopropyl fluorophosphate (DFP) and may be referred to choline esterase inhibition. Symptoms are always associated with:

(a) Decline in choline esterase activity, both in terms of acetocholine esterase ("true-" ChE) of erythrocytes and nerve tissue and in terms of the "pseudo-" ChE of serum and other tissues.

(b) Inhibition is essentially irreversible, and the recovery of normal activity depends on renewal (regeneration) of ChE.

(c) Some of these agents *per se* inhibit ChE being active *in vitro* and *in vivo*, for example, TEPP, para-oxon, DFP. Others, such as OMPA, EPN®, parathion and malathion are inactive (or relatively so) *in vitro* and are activated in the body to substances which inhibit ChE both *in vivo* and *in vitro*.

(2) Blood choline esterase levels in animals may be depressed to less than 20% of normal before symptoms of systemic poisoning appear.

(3) Symptoms may be grouped in three categories as follows:

(a) *Muscarinic symptoms*: (Action on post-ganglionic cholinergic nerve elements and excessive stimulation of autonomic effector cells); early signs = anorexia, nausea; followed by vomiting, abdominal pain and cramps (gastro-intestinal hypermotility), sweating, salivation, tears; diarrhoea, heart spasm, dyspnoea; finally deep pallor, miosis, lung oedema, cyanosis, anal and urinary incontinence. Atropine antagonizes or minimizes the foregoing symptoms and gives at least partial premunition against them.

(b) *Nicotinic symptoms*: (Action on preganglionic and somatic motor nerve elements yielding, at first, intense stimulation, and, later, paralysis of voluntary [striated, skeletal] muscle): Early signs = twitching of muscles in tongue, eyelids; muscle twitching spreads, engulfing facial, neck, eye-surrounding muscles; finally, deep, general muscular twitching of skeletal muscles followed by weakness, flaccidity, paralysis. Atropine is ineffective against these symptoms. No known antidote.

(c) *CNS symptoms*: (Direct action on central nervous system, comprising initial stimulation and, finally, deep depression of activity): Early signs = headache, giddiness, tension, apprehension, foreboding; later (in serious poisonings) ataxia, general deep tremor, drowsiness, mental confusion, slurring and other speech difficulties, convulsions, loss of reflexes and sphincter control, coma. Atropine is effective in control and gives premunition against these symptoms.

(d) Experimental poisoning of animals reveals that various degrees of heart block and arrest may occur (compare with the action of acetylcholine and vagal stimulation on the isolated heart).

(e) Following ingestion with suicidal or homicidal intent, organic phosphorus insecticides have yielded virtually instant death. However, even the most serious symptoms (observed only in advanced cases) do not foreclose favorable recovery with continued, constant and vigorous treatment of the proper kind both specific (full atropinization) and supportive. The patient must be constantly under watch. The emergency (even with favorable initial response to treatment) endures for many hours (24 to 48 hrs at least) and relapse may occur with waning atropinization and continuing nicotinic effects.

(f) The immediate cause of death is apparently respiratory failure and it should be remembered that the muscular weakness which brings this about is not guarded against by atropine. Oxygen, under slight positive pressure, is recommended early. Never walk the victim; avoid morphine.

(4) Variations in toxicity, response to, and symptomatology of organic phosphorus insecticides: [1837,745,493,2699,497,2231,353,89,714,237,851,1221,713,3010,1846,1755,1089,27,2044]

(a) N.B. Mean choline esterase values for normal human beings, unexposed to any organic phosphorus toxicants, have been determined to range as follows:

Erythrocyte choline esterase: 0.67 - 0.86 Δ pH units/hour.
Plasma choline esterase(s): 0.70 - 0.97 Δ pH units/hour.

Values of <0.5 for either system represent, for most persons, an abnormal depression of activity. However, values as low as 0.2 or less do not necessarily yield overt symptoms. This last obtains particularly for persons exposed to organic phosphates daily over weeks of time, but with individual exposures kept at minimum. Such persons are, of course, in critical danger from any enhanced or acute exposure. Although some liver diseases reduce ChE activity, these ailments preclude an active working life. ChE depression, at the moment, is largely due to exposure to organic phosphorus agents. Not all the symptoms described above are necessarily observed in any single case; toxicant, route, vehicle, etc., all play their part in imposing variation.

(b) The symptoms generalized above result from choline esterase inhibition in various parts of the body. The organic phosphorus insecticides, despite their number and structural diversity, as a class focus their action with great uniformity on this enzyme system. However, groups of these compounds and individual members reveal some differentiating nuances of action, emphasis, toxicity and symptoms.

(1) Each organic phosphorus insecticide does not produce precisely the same symptoms (nor symptom sequences) as the others.

(2) Diversity of structure and physical properties are reflected in differences of toxicity, speed of action, emphasis of action at particular sites, etc., even though the ultimate effects produced are referable to choline esterase inhibition. Some factors of diversity:

I) Tissue and site of distribution due to solubility characteristics of an agent toward water and lipids. DFP, for example, (oil/water partition coefficient = 9.5) enters the nerve axon (crab nerve) swiftly to abolish conduction at a ChE activity 20% of normal. TEPP (oil/water partition coefficient 0.14) which is highly water soluble and very active vs. ChE in vitro does not enter the axon but acts on synaptic ChE.

II) Stability of the toxicant to hydrolysis in aqueous media.

III) Resistance or susceptibility of the toxicant to in vivo detoxification.

IV) Convertibility of the toxicant in vivo to a substance more effective than the parent agent in ChE blocking. OMPA, for example, is virtually inactive toward ChE in vitro but in vivo is converted to a phosphoramide oxide with an enzyme inhibiting power vs. ChE ca. 1,000,000 times that of the parent. The same in vivo alteration holds for BFPO and Isopestox® among aminophosphates. Further examples: The thionophosphate parathion and the thionophosphonate EPN® are inactive in vitro but are converted into potent ChE inhibitors in vivo.

V) Affinity or relative specificity of the toxicant for particular esterase types, such as acetocholine esterase or pseudo-esterase(s). For example, Isopestox® (bis-isopropylamino fluorophosphine oxide) is potent in vitro vs. choline esterase but with a marked pseudo-enzyme affinity; ID_{50} pseudo-ChE=3.8 x 10^{-8} M, true-ChE=1.5 x 10^{-4} M.

VI) Ease and speed with which a toxicant reaches the action site(s) before being markedly altered, detoxified, or segregated in nonsensitive tissues or organs. For example, the lethal doses of TEPP and para-oxon are only slightly less by intravenous than by subcutaneous administration; by either route death ensues in 10-30 minutes. Parathion, methyl-parathion or isopropyl-parathion, given in ethanol intravenously or intraperitoneally yield death in one hour, but subcutaneously 10 times the average ip or iv dose must be given to kill and death does not come for 24-48 hours in case of the first two compounds and may be delayed for 10-14 days in case of the last. It is suggested that the compounds remain in the lipoids of the injection site, and are released slowly.

VII) Degree of reactivity of the toxicant with ChE and degree of irreversibility of the toxicant-enzyme complex *in vivo*. For example, some reversibility of the TEPP-ChE complex is suggested *in vivo* while the DFP-ChE complex appears completely stable and irreversible.

VIII) Ability of the toxicant to reach some action sites while being for some reason apparently excluded from others. For example, OMPA (with no appreciable anticholinesterase action *in vitro*, but convertible *in vivo* to a potent inhibitor) has, *in vivo*, slight if any CNS action, being unable apparently to gain access to the brain. Cholinergic action of OMPA seems limited to peripheral tissues, with high activity in the ileum, serum and skeletal and sub-maxillary muscles. The same appears true of BFPO. DFP, TEPP, para-oxon, parathion by contrast, reduce brain ChE as well as erythrocyte, plasma and submaxillary ChE decidedly, with better penetration of nerve tissue suggested as a mechanism.

IX) Among species (and sexes of species) there are differences in susceptibility to organic phosphorus toxicants. For example, parathion appears more toxic for female than for male rats (although both sexes appear equally susceptible to TEPP, para-oxon, and some parathion-isomers). EPN® and Potasan® exhibit sex differences in toxicity. Male rats appear more susceptible than females for OMPA and Mipafox®. It is suggested that in case of toxicants which require metabolic conversion to express their toxic potential the sex differences in susceptibility reflect the ease and efficiency of conversion inherent to the individual sexes.

(5) Histopathological evidences of organic phosphorus compound poisoning:
[2336,142,720,2218,1600,190,241,2891,2892,1843,2493,2894,892,265]

(a) Similarities have been noted between the effects of certain organic phosphorus toxicants and tri-o-cresyl phosphate (TOCP). For example, Isopestox® (bis-isopropylamino fluorophosphine oxide) poisoning in human beings gave two near deaths in flaccid paralysis resembling "ginger jake paralysis."

(1) DFP, Isopestox®, TOCP are notable for a selective anti-pseudocholine esterase action.

(2) DFP, Isopestox®, TOCP in single and chronic dosage have produced paralysis in animals such as chickens and rabbits.

(3) In the case of TOCP poisoning characteristic nerve lesions have been observed namely: Demyelination of peripheral nerves, anterior horn cell degeneration and fatty degeneration of spinal cord white matter. These structural changes succeed the rapid decline of pseudo-ChE which precedes clinical signs by some 2 weeks.

(4) Isopestox® and DFP have produced lesions similar to those of TOCP, with demyelination and with spinal cord lesions more severe than peripheral nerve lesions. Para-oxon, iso-OMPA and tetraisopropyl pyrophosphate have not yielded this histopathology.

(5) The demyelination (and other histopathologies) do not appear to be consequences of pseudocholine esterase inhibition but rather to be concomitant effects. A curious association between anti-pseudocholine esterase specificity, or affinity, and the histopathology described remains unexplained.

(6) The organic phosphorus insecticides as chronic toxicant agents:

(a) These compounds are toxic to higher animals (and man) by any portal of entry. 1458

(b) Detoxified in the animal body with relative swiftness, these compounds are not stored or accumulated appreciably in the body.

(c) However, in repeated or chronic sub-acute exposure the decline in choline esterase 857
activity is progressive and in time may reach dangerous and also fatal levels. 1458,713

(1) This last follows on the fact that the inhibition of ChE by these compounds is ir- 857
reversible (or virtually so) and that the rate, degree and intensity of inhibition at 713
certain exposure levels outstrips the rate of (and capacity of) regeneration in and by 2231
the body, for instance parathion, given to rats at 0.5 mg/k/day, exerted no appreciable 1458
cumulative action on choline esterase, but at 3 mg/k/day was uniformly fatal to all subjects after 10 days of exposure.

(2) Summary of chronic toxicity, organic phosphorus insecticides: 1057,1462
TEPP: (20% formulation) at 1000 ppm in diet for 12 wks, rats: No overt symptoms. 1953,743
Parathion: Symptoms of varying severity at 25, 50-100 ppm in diet. 188,1553
OMPA: Rats at 1 mg/k/day ip: 100% kill; at 0.5 mg/k/day: Ca. total depression of 1961,854
red cell ChE; at 10 ppm, 52 weeks in diet: Brain ChE ca. total depression; 1610
at 1, 3, 10 ppm plasma and red cell ChE variously depressed; at 0.3 ppm little effect.

NPD: Rats at 60 ppm: No overt signs; at 180 ppm: Overt signs but no pathology in 1 yr. exposures.

EPN®: Rats at 50, 150 ppm (♂♂), 25, 75 ppm (♀♀) for 2 yrs: No overt signs; dogs for more than at 1 yr 0.1-1 mg/k/day: No depletion of erythrocyte ChE. Rats have tolerated, sans symptoms, 180 ppm.

Malathion: Rats at 5000 ppm in diet, 2 yrs: No increase in mortality, no histopathology; at 1000 ppm red cell and plasma ChE moderate depression; at 5000 ppm marked depression.

Systox® : Rats at 10, 25 ppm: Marked depression erythrocyte ChE; at 50, 100 ppm: Depression of red cell and plasma ChE; 50 ppm have yielded overt symptoms.

Diazinon: Rats at 25-250 ppm in diet 1-2 months: No overt signs; dogs at 1 mg/k/day for 1-2 months: Profound decline in blood ChE.

Chlorthion®: Rats: 200 mg/k/day intolerable for more than 5-10 days; ChE depression swift and profound; 50 mg/k/day depressed ChE by 50% but was tolerated for 60 days.

Acute oral and dermal LD_{50} values of organic phosphorus insecticides for white, laboratory rats: 90

Substance	LD_{50}, oral, (mg/k)		LD_{50}, dermal, (mg/k)	
	♂♂	♀♀	♂♂	♀♀
Chlorothion®	880.0	980.0	1500;4500	4100.0
Demeton (Systox®)	6.2	2.5	14.0	8.2
Diazinon	108.0	76.0	—	180.0
Dipterex®	630.0	—	—	—
Malathion	1375.0	1000.0	4444.0	4444.0
Parathion	13.0	3.6	21.0	10.9
TEPP	2.0	1.2	—	—
For comparison: LD_{50} values for white rats certain halogenated-hydrocarbons				
Chlordane	335.0	430.0	840.0	690.0
Chlorobenzilate	1040.0	—	—	—
DDT	113.0	118.0	—	2510.0
Dieldrin	46.0	46.0	90.0	60.0
Dilan	—	—	6900.0	5900.0
Endrin	17.8	7.5	—	15.0
Lindane	200.0*		500.0	—
Methoxychlor	6000.0*		—	>6000.0
Toxaphene®	90.0	—	2300.0	80.0

*Sex not specified.

Approximate (average) single LD (oral) for white ♂ laboratory rats: 185

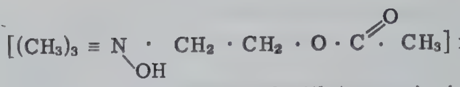
Substance	Average Single LD (mg/k)
TEPP	2
Para-oxon	2
Dimefox®	5*
OMPA (Schradan)	10*
Parathion	15**
Systox®	15
Potasan®	25**
EPN®	40**
Malathion	<1000

*♀♀ considerably > susceptible. **♀♀ somewhat > susceptible.

(d) Obviously any of this class of insecticides is toxic, damaging and fatal at appropriate doses whether single, repeated, or chronic. However, toxicity (for degree of damage) following single or repeated exposure is to be distinguished from hazard (either acute or chronic), which is an estimate of potential harm which might follow under the ordinary conditions of use. Viewed in this light, this class of toxicants is no more forbiddingly dangerous (when properly employed) than such substances as nicotine, HCN, various arsenicals, etc., which have for years been routinely employed in pest control on a widespread scale. 1458

(7) Summary; interpretations: 851,1221

(a) As choline esterase inhibitors, the organic phosphorus insecticides are parasympathomimetic drugs, acting upon the tissues and structures innervated by cholinergic nerves. Muscarinic and nicotinic effects are components of their action and their effect is conversely antagonistic to curare. The complexity and far-reaching nature of their effects (leaving aside all the nuances of chemical difference between the agents, dosage, species differences, route and vehicle, metabolic fate, etc.) are to be appreciated only by some attention to the essential neurohumoral agent whose pharmacodynamic action they so closely imitate namely acetylcholine. Indeed, the effects of these agents are in large part ascribable to acetylcholine itself, since they favor its accumulation and "un-physiological" action by disrupting the enzyme mechanism which controls, regulates and holds within bounds the action of acetylcholine upon effector cells. However, it must be kept in mind that anti-choline esterase agents may have also some direct action upon effector cells. The possibility that this last may be a component of their action may add further nuance to their effects.

(b) Acetycholine  $[(CH_3)_3 \equiv \underset{OH}{N} \cdot CH_2 \cdot CH_2 \cdot O \cdot \overset{O}{C} \cdot CH_3]$ is one of the two principal substances, the other being epinephrine, concerned with transmission of the nerve impulse at synapse and junction of nerve and effector.

(1) Present in the tissues as a non-diffusible, physiologically inactive form as precursor, or bound-acetylcholine not susceptible to choline esterase hydrolysis, acetylcholine in its active form is released by an appropriate nerve impulse.

(2) Acetylcholine is known by direct experimental evidence to be released by stimulation of the cranio-sacral autonomic nerves to smooth and cardiac muscle and to exocrine glands, whereupon it acts upon effector cells to elicit their characteristic response to stimulus.

(3) In normal (physiologic) function the action of acetylcholine at a given point is of brief and controlled duration since an esterase in the tissues hydrolyzes it to acetic acid and choline. Choline, depending upon action site etc., is from 500-100,000 times less active physiologically than acetylcholine. Many of the esters of choline are hydrolyzed by choline esterase.

(4) Acetylcholine precursor, choline esterase and choline acetylase are present in skeletal muscle, smooth and cardiac muscle and in nearly all parts of the nervous system (being particularly abundant in autonomic ganglia and at skeletal muscle end plates.)

(5) Exogenously administered, acetylcholine produces in effector cells responses reproducing exactly the stimulation of cholinergic nerve elements. The pharmacologic action is muscarinic, nicotinic and curariform. Small doses of acetylcholine (and of choline esterase inhibitors) are, like nicotine, excitatory to effector cells but large doses are depressant. This duality is notable in ganglion cells and skeletal muscle fibers.

(6) The stimulant or depressant action of acetylcholine is on the effector cells themselves, and not on nerve endings. Acetylcholine stimulates: I) All effector cells innervated by preganglionic parasympathetic and sympathetic nerves and all cerebro-spinal somatic motor nerves to skeletal muscle; II) post-ganglionic parasympathetic and "sympathetic" nerve-supplied effector cells such as sweat gland cells and certain blood vessels. In large doses it blocks (depresses) the effectors mentioned in (I). Acetylcholine cannot be strictly characterized as a parasympathomimetic or sympathomimetic agent, since it is itself the chemical agent liberated by post-ganglionic autonomic nerve stimulation. Blocking agents do not suppress or interfere with the release of acetylcholine. The site of action of autonomic blocking agents is peripheral to the site of acetylcholine release at the neuroterminals.

(7) Action of acetylcholine on sweat glands and in vasodilatation of certain blood vessels was once thought anomalous, these elements being deemed "sympathetic" in innervation. Although the neural elements involved traverse "sympathetic" pathways, they are functionally parasympathetic, and their impulses release acetylcholine at the periphery.

(8) Ganglion cells are excited by the release of acetylcholine when pre-ganglionic impulses reach the synapses in the ganglia. All pre-ganglionic impulses stimulate ganglion cells and acetylcholine is the mediator. I) Small amounts of acetylcholine (e.g. 25 μg/cc in perfusion media discharge the superior certical ganglion, while 100 μg/cc elicits ganglionic blockade, with the preganglionic impulses no longer effective) discharge ganglion cells. Precursor-acetylcholine and acetocholine esterase are demonstrable in ganglia.

(9) Somatic motor nerve impulses bring about release of acetylcholine at the end-plate terminals; the acetylcholine so released mediates transmission of the impulse to the skeletal muscle fiber effectors to yield the response. When the choline esterase of skeletal muscle is inhibited (or blocked) release of acetylcholine, following motor nerve stimuli, is not impeded and there results repetitive discharge with quick, twitchlike muscle contraction, the muscle being specifically excitable at the end plate region. In normal skeletal muscle functioning minute, but adequate, amounts of acetylcholine are liberated in response to somatic nerve impulses to skeletal muscle. This acetylcholine is intimately concerned with transmission of the excitatory process at the myoneural junction. Choline esterase functions swiftly to hydrolyze the released acetylcholine, thus limiting and so to speak, keeping the response in "physiologic" bounds.

(c) Less clear cut than in the case of skeletal, smooth, and cardiac muscle, exocrine glands, etc., is the role of acetylcholine in central synaptic transmission in cord and brain. A role is decidedly suggested by the presence of bound acetylcholine and choline esterase in the CNS.

(1) Acetylcholine alone (or combined with anti-choline esterase, for example eserine) both stimulates and depresses (depending on dose, species etc.) various functions of the cerebrospinal axis.

(2) Anti-choline esterases such as organic phosphorus insecticides excite and depress various central functions; the action is enhanced by concomitant acetylcholine administration. Under anti-choline esterase administration, acetylcholine increases in the cerebral cortex and the effect is thought to be either on the mediator or the cells themselves in whose function acetylcholine plays some essential role.

(d) Consideration of choline esterase is an essential corollary of a consideration of acetylcholine in the mechanism of neural transmission. True, or specific choline esterase, i.e. acetocholine esterase (or acetylcholine esterase) has been found in nearly all parts of the nervous system. In addition, pseudo-choline esterase(s), or non-specific choline esterase(s), is (are) present in various tissues and fluids.

(1) In the gastro-intestinal tract the inhibition of the pseudo-choline esterase normally present enhances tone and motility of the gut because of accumulation of endogenously liberated acetylcholine. Inhibition of the pseudo-choline esterase accounts for the gastro-intestinal symptoms of organic phosphorus insecticide poisoning namely: Nausea, vomiting, cramps, diarrhoea and incontinence which are linked to excessive motility and peristalsis.

(2) Whatever the difference in the roles of true or acetocholine esterase(s) and pseudo-choline esterase(s), in case of their inhibition or blockage acetylcholine is protected from hydrolysis, and its action is prolonged and intensified even to the jeopardy of life.

(e) There has grown a general concept of a cholinergic division in the nervous system. To the category "cholinergic nerves" belong those nerve elements whose impulses result (at their terminals) in the liberation of acetylcholine. It comprises all post-ganglionic parasympathetic elements and autonomic (sympathetic or parasympathetic) preganglionic elements. Included are preganglionics to the adrenal medulla, anatomically "sympathetic" fibers to sweat glands and some blood vessels, somatic motor nerves to skeletal muscle and to intrafusal fibers in mammalian skeletal muscle spindles.

(1) The field of action of acetylcholine, then, takes in all ganglia, skeletal muscle, the adrenal medulla, smooth muscle, cardiac muscle, and such exocrine glands as sweat, lacrimal, salivary, and mucous glands.

(2) In consideration of the symptoms of poisoning and the pharmacological effect of the organic phosphorus insecticides acting through inhibition of choline esterase the above field of action is suggestive.

(3) Effects of acetylcholine (as of organic phosphorus toxicants) are: I) Muscarinic (action on visceral autonomic effectors, smooth and cardiac muscle, exocrine gland cells;) II) nicotinic (and like nicotine, which initially stimulates and then paralyzes autonomic ganglia and skeletal muscle, acetylcholine stimulates ganglia, skeletal muscle and CNS in low concentration, while paralyzing the same in high concentration).

(4) Atropine blocks the muscarinic action, whether excitatory (in the intestine) or inhibitory (in heart muscle). Atropine is less effective, however, in blocking the muscarinic action of acetylcholine at those sites where it appears to be released within the effector cell(s) for example the motor end plates in the muscle fibers.

(5) Suggestive, in considering the action of organic phosphorus insecticides on higher animals, are the following high-lights of acetylcholine action:

I) Cardio vascular action: Vaso-dilatation with fall in blood pressure. Cardiac arrhythmias such as bradycardia, depression of the atrial (auricular) muscle, the auriculo-ventricular node and the conducting bundle of His.

II) Gastro-intestinal action: Increased tone, contraction amplitude, and peristalsis in stomach and intestine; stimulation of secretions of gastro-intestinal exocrine elements.

III) Exocrine action: Stimulation of glandular secretory action of all exocrine gland cells with a cholinergic postganglionic innervation such as salivary, sweat and lacrimal glands.

IV) Respiratory action: Bronchospasm and gland secretion from the bronchial tree. Collection of fluid and mucus in lungs and bronchial elements.

V) CNS action: Respiratory stimulation followed by depression due to central nervous action.

VI) Skeletal muscle action: Rapid, asynchronous fasciculation and tremor, followed by exhaustion and paralysis.

(8) Some general toxicological considerations of organic phosphorus insecticides; hazard, precautions etc.

(a) While the toxicity of these compounds may have been at times exaggerated they do, in 1458
general, present the constant danger of serious illness or death to those who come in con- 1221
tact with them, particularly without proper precautions to prevent entry into the body via mouth, skin or lungs.

(1) There is every expectation that mammalian toxicity will be reduced while preserving 1461,1848
insecticidal, acaricidal effectiveness for example, malathion. 860,2392

(b) Although these compounds act as potent and irreversible inhibitors of choline esterase, 1221,714
in vitro anti-choline esterase activity is not an entirely reliable guide in evaluation of 237,3357
mammalian toxicity. For example, OMPA has almost no in vitro activity but is con- 443,3316
verted in vivo to an active ChE inhibitor. 716,3205

(1) In general, cholinergic symptoms (rabbit, monkey) such as muscle tremor, miosis 2799,2153
and diarrhoea are associated with low true-choline esterase activity (erythrocyte 2155,2156
and brain acetocholine esterase) and death occurs at zero brain ChE activity (DFP 1631,187
poisoning). 714,2099

(2) Pseudo-choline esterase (monkey, man) in DFP poisoning may decline to as low as 1057,1280
1% of normal with but slight effect, if any.

(3) Only tissue choline esterase levels, for example, erythrocyte ChE are significant in interpreting the action of these compounds.

(4) Whole blood (red cell ChE) choline esterase levels are the all important guide. Lowered ChE activity leads to increased sensitivity and, consequently, to increased hazard from subsequent absorption of an anti-choline esterase toxicant. Symptoms of early phosphorus insecticide poisoning are common enough (headache, nausea) but red cell ChE level is important and essential to a differential diagnosis. Also, some regrettable experiences with delayed effects in poisonings with Isopestox,® i.e., flaccid paralysis and near-death in the 3rd week after the acute phase, warn against the assumption that there will be no sequelae if the acute effects are mastered. This last is particularly true in repeated exposure with persistent depression of blood ChE. Among factory workers involved in synthesis, formulation, etc., of these insecticides, it has been recommended that ChE levels be followed routinely in spite of precautions against absorption, since ChE may decline to critical levels without overt signs or complaints. Low ChE warns of impending toxicity. Establishment of normal human ChE levels has constituted a problem.

(5) Atropine, effective against acute muscarinic signs is not effective in case of large doses. Overwhelming doses defy antidote. Parasympathetic nervous activity is the warning of excess exposure calling for atropinization, removal from chance of further exposure until ChE regeneration is accomplished and proper supportive measures.

(c) Sub-acute exposure is probably a more pressing consideration in absence (especially among persons applying these toxicants) of precautions involving such things as careful ventilation, respirators, protective clothing, personal sanitation and care not to eat or smoke if contamination possibilities exist.

(1) It is important to make periodic determinations of ChE activity in those occupationally exposed and to watch for such warning signs as giddiness, chest tightness, nausea, blurred vision, intestinal cramps and diarrhoea. Accidents among pilot spray applicators in flight have been laid to these toxicants which have impaired judgement and induced blurred vision and otherwise reduced pilot efficiency in sub-acute exposures.

(d) Chronic toxicity constitutes a hazard for manufacturing, formulating and application 1458,714
personnel differing from sub-acute exposure only in degree and the time needed for 241,2891
development of overt signs. 1843,2493

(1) Animals, too, reveal danger signs which are a safety factor in chronic exposure among them refusal of food, a generally toxic state and inability to eat.

(2) Breaking off all chance of further exposure is essential at the first sign of toxicity. This is usually followed by recovery in both man and animals without residual pathology. Animals, even with ChE at low levels, resume eating and appear normal in a few days after cessation of exposure.

(3) Recovery from acute and sub-acute exposures may be expected with application of proper remedies.

(4) The consumer is not exposed to any grave chronic hazard. Under proper use these toxicants are low in residual hazard generally speaking. After from 1 to 3 weeks, depending on crop and toxicant, little significant residue remains of the materials now current. Prior evaluation is, of course, essential.

(e) Hazard exists for manufacturing, formulating, and applying workers and is real and insistent unless precautions and safety measures are in rigorous force.

(9) Metabolic fate of organic phosphorus insecticides in higher animals:

(a) DFP (di-isopropyl fluorophosphate) is rapidly absorbed from the gastro-intestinal tract 2149,562
and after parenteral injection. It is detoxified by an enzyme (unrelated to phosphatase 851,1221
or choline esterase) which is present in plasma, erythrocytes, kidney, liver, etc.

(1) Hydrolysis occurs to dialkyl phosphoric acid, H$^+$ and F$^-$, particularly, in liver.

(2) In man, 60% to 70% of injected DFP appears in the urine as di-isopropyl phosphate in the first 10 days.

(b) Parathion: p-Nitrophenol is the principal metabolite, appearing with p-aminophenol in 2308,1112
the urine in sub-toxic doses not productive of symptoms but with decline in plasma 1989,3215
ChE.

(1) Does not appear in milk, blood or urine of cows fed forage at residue levels much 681
greater than those on field treated forage. 2437

(2) S^{35} labelled (in rabbits): S^{35} appears in urine promptly after dosage cutaneously or 1694
intravenously. S^{35} is not stored and appears not as parathion but as a metabolite. 1693

(3) Transformed in vivo to the oxygen (orthophosphate) analogue (para-oxon) the S^{35} being 794
freed. The fate of the phosphate is undetermined. S is excreted in urine and the 2243
aromatic nitro-portion is excreted as p-nitro- and p-amino- phenol.

(c) Para-oxon: Reported to be enzymatically hydrolyzed by liver slice preparations in vitro 27
to metabolites non-inhibitory of ChE.

(d) While there exists little detailed information on the metabolic fate of the organic phos- 328,391,27
phorus toxicants in higher animals there is enough information to suggest that a good 306,1683
proportion of any of these compounds is in vivo metabolized enzymatically to an 1089,1846
inactive state before there is ever much opportunity to block choline esterase. In 2335,493
view of the size of the doses needed to kill (and if the reaction of toxicant and choline 859,1109
esterase is, as claimed, on a mole for mole proportion) much of the intake must find 1790,531
another outcome than choline esterase blockade. 497,1416
30,795,1090

(1) However, in regard to the preceding, it must be remembered that some organic phosphorus insecticides in the course of their metabolic transformations in vivo become at one stage or another far more effective anti-choline esterase agents than is true of the original compound when this is tested in vitro. The thionophosphates, for instance, parathion, are changed to phosphates active against ChE. In the case of parathion the active substance is probably para-oxon. OMPA, inactive vs. ChE in vitro, is converted by mammalian liver (in vitro and in vivo) to an active anti-ChE agent. The transformation is enzymatic in vivo and may be brought about chemically in vitro with permanganate. The reaction is an oxidation which transforms one of the amide nitrogens to a functional group, phosphoramide N-oxide. Brain, kidney and heart muscle in vitro systems do not effect the transformation done by liver which is probably the sole conversion site in vivo since hepatectomy protects rats against OMPA. (See the section devoted to octamethyl pyrophosphoramide [OMPA] for details of the proposed pathway of conversion). A similar transformation of OMPA by plant tissue is reported. The phosphoramide oxide proved the best ChE inhibitor of the transformation products while with products of further oxidation, maximum inhibition of chymotrypsin could be obtained. BFPO [bis-(dimethylamino) fluorophosphine oxide] is activated by a similar oxidation with permanganate to a product whose ID_{50} is 4×10^{-8} M (human serum ChE) as compared with 3×10^{-3} M for BFPO.

(e) Sex differences in rats with respect to susceptibility to organic phosphorus toxicants have 713
been noted above. The difference between ♂♂ and ♀♀ is marked for parathion, diethyl-4-methyl-7-hydroxycoumaryl phosphorothionate, p-nitrophenyl benzene phosphorothionate (EPN®), OMPA and N,N'-diisopropyl phosphorodiamidic fluoride (Mipafox). No sex differences in susceptibility to TEPP, para-oxon and two isomers of parathion have been noted.

(1) The compounds showing the marked sex differences in toxicity are precisely those requiring metabolic activation to active anti-ChE substances. The difference in susceptibility of the sexes, it is suggested, may lie in the ease and efficiency of the conversion, these being greater in the more susceptible sex.

(f) Evidence of metabolic activation in a comparison of erythrocyte choline esterase inhibition 30
by toxicants administered to an animal in vivo and incubated in vitro with blood from the same animal:

Toxicant	Dose (mg/k)	Route	Time After In Vivo Injection Or Incubation (min.)	% Erythrocyte ChE Inhibition	
				In Vitro	In Vivo
Parathion	10	iv	10	8	83
"	10	ip	11	9	66
"	10	ip	40	20	81
Potasan®	15	iv	20	26	94
"	15	iv	30	—	97
Methyl-parathion	10	iv	10	—	67
"	10	iv	40	8	64
"	15	iv	10	6	80
"	15	iv	40	5	65
Isopropyl-parathion	15	iv	10	21	34
BFPO	20	iv	7	31	88
"	20	iv	20	—	86
"	20	iv	42	—	89

III) PHARMACOLOGICAL, PHARMACODYNAMIC, PHYSIOLOGICAL, ETC., CONSIDERATIONS OF ORGANIC PHOSPHORUS TOXICANTS IN INSECTS:

1) General Remarks: [Refs.: 2231,353,713,2773]

a) The organic phosphorus insecticides are effective against insects and acarines by contact, ingestion or fumigant action. In addition some (as "systemic" insecticides) absorbed by the tissues and juices of plants, via roots or aerial parts (leaves, stems, trunk, bark) kill by ingestion or fumigant action insects feeding on such treated plants or resting thereon. "Systemic" insecticidal action may reside in the compound in the form in which it was originally absorbed by the plant or after metabolic or other alteration within the plant.

(1) Penetration of insect cuticula is highly efficient. Topical and injection LD_{50} doses are for many com- 206
pounds about equal although species differences may also be striking. Site of topical application may 2244
affect speed of action depending on nearness of the site to the central nervous system of the insect. 166

(2) The vehicle or solvent may influence cuticular penetration to a degree.

b) Once having gained entrance to the insect body, organic phosphorus toxicants are rapidly disseminated 989,2657
through the tissues. 2034

(1) Transport is evidently rapid and complete via the haemolymph.

(2) Some parts of the body, for instance foregut, show high efficiency in segregating the toxicants from the haemolymph.

c) Metabolism rate shows correlation with readiness of hydrolysis on the part of a given toxicant.
   (1) While the insect CNS is deemed the primary action site of ChE inhibition due to the toxicant or its metabolic products the amount recoverable from the CNS is usually very small in terms of the total amount administered.

2) Toxic action of organic phosphorus insecticides on insects:
   a) Choline esterase inhibition is most generally offered in explanation of the principal toxic action on the assumption that the mechanism of nerve conduction and impulse transmission is similar in mammals and insects. 2342,505 864,2244 1755,713 170,2044 1584
      (1) Assumed also is the presence and indispensability of choline esterase(s) in insect conducting tissues and the importance of acetylcholine (or some highly similar substance(s)) as a chemical mediator of neural impulse transmission between nerve and effector.
      (2) Inhibition of insect choline esterase(s) (and indeed other esterases) by the organic phosphorus toxicants is well authenticated.
      (3) Good correlation between mortality and degree of ChE inhibition, and between anti-choline esterase activity and insect toxicity, has been reported for many of these compounds.
   b) The overt signs of poisoning in Periplaneta americana using DFP and TEPP are like those which follow physostigmine (eserine) injection, namely: 505,1221 851
      (1) Hyper-excitability, hyperactivity, almost immediate and followed by:
      (2) Hyper-reflexia, exaggerated tonus giving way to:
      (3) Ataxia, lack of muscle coordination and orderly activity passing to:
      (4) Tonic and clonic convulsions ending at last in paralysis and death. Recovery from the convulsive state induced by DFP is rare but recovery from TEPP-induced convulsions may occur. (DFP is notable for irreversibility of ChE inhibition while in vivo reversibility of TEPP ChE-inhibition, at least in some degree, is known).
   c) Following perfusion with DFP at 6 x 10^{-4} M strong after discharges were recorded from giant fibers of the Periplaneta ventral nerve cord after single preganglionic stimulus. Synaptic block (reversible) may follow. 2683
      (1) Giant fiber axonal conduction was not influenced by DFP at 5 x 10^{-3} M.
      (2) Application of acetylcholine (5 x 10^{-6} M) after pre-treatment with DFP (10^{-5} M) yielded immediate synaptic (but not axonal) block. HETP reproduced the above activity of DFP.
      (3) Ganglionic synaptic facilitation followed by blockade attended application of DFP (5 x 10^{-5} M) and TEPP (3 x 10^{-7} M) to the 6th abdominal ganglion of Periplaneta. Axonal conduction was extinguished only by DFP at 6 x 10^{-2} M and TEPP at 3 x 10^{-3} M. 2682
      (4) TEPP at 30 µg to Periplaneta leg yielded in the crural nerve (1 to 2 hours after treatment) a repetitive discharge enduring for ca. 20 minutes. Parathion induced the same response after a longer time but OMPA did not produce the action after passage of 4 post-treatment hours. 520
      (5) TEPP at 1 µg by injection to Blattella yielded immediate enhancement of respiratory rate attaining 3-fold the normal in ca. 1.5 hours; subsequently, with onset of paralysis the respiratory rate declined until death. Parathion yielded a similar effect but with a 1 hour latent period before respiratory rate upsurge. Parathion also stimulated the Periplaneta heart to more rapid pulsation with ultimate systolic halt. 2421
   d) Acting in in vitro systems containing Periplaneta coxal muscle cytochrome oxidase, stimulation was observed (notably with TEPP) at either 10^{-3} or 10^{-5} M. Of the 4 tested (TEPP, OMPA, Malathion, Parathion) only the last two yielded complete inhibition at 10^{-3} M. Activity was measured by O_2 uptake of the preparations in Warburg's apparatus. 2305

3) Mechanisms of organic phosphorus toxicant action in insects.
   a) Although some contend that the physiology of the insect nervous system differs from that of mammals in that neither esters of choline nor epinephrine (adrenaline) are concerned in it, others claim an essential similarity based on the presence of much acetylcholine and choline esterase(s) in insect nerve systems. The role of acetycholine-like materials in insect nervous transmission is sustained by others. The data: 1583,1584 2339,988 509,3096 2539,2245 138,2682 1984
      (1) Compared with mammals, the toxic doses of choline esters for insects are very high: acetylcholine= 7-10 mg/g, carbachol=1 mg/g for Periplaneta, which also tolerates 20 mg/g of acetyl-β-methylcholine without effect. 1583 3096
      (2) As among higher animals specific differences have been found in the choline esterase(s) from various insect species. 504,153,503 2658,2245
      (3) Enzymes active against non-choline esters are also known from insects. 2043,2045
      (4) Choline esterase from nerve tissue of some insects appears to resemble closely the "true" or acetocholine esterase of mammals. 2342
      (5) In Tenebrio larvae a non-acetylcholine-hydrolyzing esterase, acting on ethyl butyrate and o-nitrophenyl acetate, is inhibited by TEPP or parathion. A similar o-nitrophenyl acetate-hydrolyzing-enzyme (also TEPP inhibited) is demonstrable in eggs and active stages of Diataraxia oleracea, Ephestia kühniella, Plutella maculipennis, Macrosiphum euphorbiae, Acyrthosiphum pisi. ID$_{50}$ of TEPP for the enzyme involved = 4 x 10^{-7} M. 2043 2045
      (6) A sufficient correlation between anti-esterase activity of the organic phosphorus compounds and contact insecticidal activity, suggests an interdependence of these factors. However, esterases other than choline esterase(s) are important in considering the toxic action of these compounds. 2043
      (7) Homogenates of Locusta migratoria migratorioides thoracic nerve system hydrolyzed acetylcholine and o-nitrophenyl acetate. The hydrolysis was blocked by TEPP. 1584

(8) In tests of the following: Diethyl-4-chlorophenyl phosphate, diethyl-2-chlorophenyl phosphate, diethyl-2,4-dichlorophenyl phosphate, diethyl-2,4,5-trichlorophenyl phosphate as ① contact poisons for insects, ② by injection into Locusta and mice, ③ as in vitro inhibitors of Locusta nerve cord acetyl-esterase and horse serum pseudo-choline esterase the results were: ① Good correlation between in vitro activity vs. nerve cord acetyl-esterase and contact toxicity vs. aphids; ② poor correlation of in vitro action vs. nerve cord acetyl-esterase and injection toxicity to Locusta; ③ no correlation between horse serum pseudo-choline esterase(s) inhibition and intraparenteral toxicity to mice. These results illustrate the complex nature of the question. 1584

(9) TEPP yielded 50% inhibition of Locusta nerve cord o-nitrophenyl acetate esterase at 2.8 x 10^{-8} M and at 4.6 x 10^{-8} M inhibited (by 50%) the acetylcholine splitting activity of Locusta nerve cord. Similarity of enzymes involved is suggested, if it is not one and the same enzyme that is involved. 1584

(10) Apis and Periplaneta contain an esterase (active against several phenyl-esters) which is not blocked by para-oxon at 1 x 10^{-3} M. 2231

b) Evidences of correlation of ChE inhibition by organic phosphate insecticides with insect mortality and other data:

Compound	Route	Insect	Dose	Results, Remarks	
DFP**	Injection	Periplaneta	0.9 μg/insect	3% inhibition nerve cord ChE activity.	505
"	"	"	2.25 "	41% " "	505
"	"	"	4.5 "	53% " "	505
"	"	"	9.0 "	85% " "	505
"	"	"	18.0 "	100% " "	505
"	"	"	10.8 "	90% Kill at 1 x 10^{-4}M DFP conc. overall.	505
"	–	"	1 x 10^{-4} M	In vitro gave 100%, in vivo 95% nerve ChE inhibition.	505
TEPP	Topical	Apis*	1 μg/g	100% Kill; 90-94% brain ChE inhibited at paralysis.	2244
"	Injection	Locusta	4 μg/insect	86% inhibition esterase action vs. acetylcholine.	1584
"	"	"	4 "	76% " vs. o-nitrophenyl acetate.	1584
Parathion	Topical	Apis*	1 μg/g	100% Kill; 90-94% brain ChE inhibited at paralysis.	2244
"		Periplaneta	(hyperactive stage)	CNS ChE 54% to 74% inhibited.	
"		"	"	Leg muscle ChE 88% to 90% inhibited.	
"		"		Conduction from CNS to leg muscle continued until CNS ChE was 80% inhibited at which time axonal conduction was interferred with.	2963 2338,2342

*At the stage of hyperactivity brain ChE is ca. 50% inhibited.

**Inhibition of Periplaneta choline esterase(s) by DFP is not readily reversible; the inhibitory effect endures at least several days; at ChE activity as low as 20% of the normal, insects continued to exhibit normal behavior.

HETP:	Injection	Periplaneta	500 μg/insect:	100% inhibition nerve cord ChE activity.	505
" :	"	"	25 " :	56% " "	505
" :	"	"	12.5 " :	100% Kill; Average inhibition ChE (nerve) = 13% only.	505

c) The presence of acetylcholine and/or substance(s) acting like acetylcholine pharmacologically, in nerve tissue of insects has had much demonstration:

(1) Of acetylcholine (or something acting like it) Tenebrio molitor nerve cord contains 100-200 μg/g, 601
Gryllus domesticus brain 65 μg/g, Xylocopa violacea 200 μg/g, Periplaneta americana nerve cord 2261
70 μg/g bound and 40-200 μg/g free.

(2) Paper chromatographic evidence indicates a substance identical with acetylcholine chloride in extracts 1984
of Calliphora erythrocephala and Lucilia serricata; acetylcholine has been identified in Apis mellifera 137
and Musca domestica head extracts. 534

d) The presence of esterase(s) active vs. acetylcholine and related substances is attested in insects by numerous studies:

(1) Esterase from fly, bee and (for comparison) mouse brains hydrolyzed respectively 11, 2.5, 0.356 micromoles acetylcholine per mg brain tissue in 0.5 hours. Fly brain activity compared with Torpedo and Electrophorus electric organs. In the foregoing tests, concentration optima of the acetylcholine substrate = 10^{-2} M. 2245

(2) Musca brain activity was slight in acetyl-β-methylcholine hydrolysis, while Apis brain was highly 2245
active. O,O-di-isopropyl p-nitrophenyl thionophosphate (which is almost non-toxic to Apis and very 1846
toxic to Musca) inhibited intensely Musca brain esterase activity, but was virtually inactive vs. Apis 1089
brain esterase activity. This last may indicate that Apis is inefficient in the transformation of thio- 2335
nophosphate to phosphate to yield active ChE inhibiting substance while the fly, Musca, may be in this regard metabolically highly effective. However, it should be kept in mind that parathion [which must also undergo in vivo the change from thionophosphate (≡ P=S) to phosphate (≡ P=O) to achieve activity] is highly toxic to Apis.

4) Metabolic fate of organic phosphorus toxicants in insects:

a) No data appears to be available on this subject.

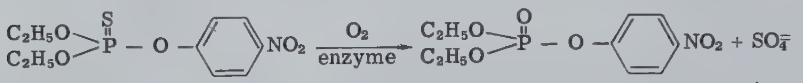
5) Conversion by insects of organic phosphorus compounds inactive in vitro vs. esterase(s) to substances active in vivo and in vitro vs. esterase(s).

a) Those toxicants inactive in vitro against mammalian choline esterase, such as Parathion, EPN® and other thionophosphates, OMPA, etc., but which are non-the-less highly toxic in vivo for mammals are toxic *in vivo* for insects also. The *in vivo* transformation of these substances to an active form is evidently effected by insect metabolism as it is by mammalian metabolism.

(1) Parathion incubated *in vitro* with *Periplaneta* nerve cord yielded a principle active vs. ChE. 509

(2) Intact tissues of *Periplaneta in vitro* supplied with O_2 converted pure parathion and methyl-parathion to 2243
active choline esterase inhibitors. Homogenization of tissue and heat to 75°C prevented the conversion. Such enzyme inhibitors as cyanide, azide, selenite, $HgCl_2$, iodoacetic acid, chloropicrin, inhibited the conversion in low concentrations. Activity of various tissues able to effect the conversion was in the following order: foregut > Malpighian tubules > midgut > nerve cord > hindgut > fat body; cuticle, muscle could not effect the conversion.

(3) Products of the conversion of parathion and methyl parathion by *Periplaneta* foregut *in vitro* are 2248
indicated to be para-oxon and methyl-para-oxon respectively. The conversion is assumed to be enzymic 2243
and is an oxidation not an isomerization reaction: 1846



(Parathion) (Para-oxon) (Sulfate)

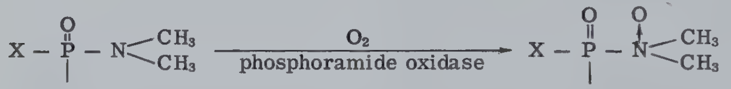
By some, fat-body has been found the most effective tissue in the conversion. The same type of activation (thionophosphate [≡P = S] to phosphate [≡P = O]) is demonstrable with malathion and EPN® .

b) OMPA (Schradan; octamethyl pyrophosphoramide) is converted to an active choline esterase inhibitor both by insects susceptible and those not susceptible to the insecticide.

(1) *Periplaneta* (for which OMPA is non-toxic) tissues *in vitro* (fat body, hind-, mid-, fore- gut, cuticulum, 2392
nerve *but not* muscle) converted OMPA to active esterase inhibitor. *Tenebrio*, *Oncopeltus* (OMPA 495
susceptible), *Anasa* (OMPA susceptible), *Vanessa*, tissues also effected the conversion.

(2) Homogenization of tissues destroyed activity although adenosine triphosphate, cytochrome -C or 2392
magnesium ion preserved some activity to homogenates. Heat characteristics and inhibiting agents 495
suggest the enzymatic nature of the conversion.

(3) Oxidation occurs at the N of a dimethyl phosphoramide group, yielding a phosphoramide oxide with 497
increase in ChE inhibitory power of 1 million-fold. In the conversion a relatively stable pyrophos- 1416
phoramide is changed to a reactive phosphorylating agent, the monophosphoramide of OMPA (Schradan). 2392
492



(OMPA) (Active monophosphoramide oxide, metabolite)

The phosphoramide oxide is readily hydrolyzed and, as usual, ease of hydrolysis is associated with anti-ChE activity. The conversion is apparently identical in insects, mammals, plants and micro-organisms (yeast, bacteria). BFPO [bis-(dimethylamino) fluorophosphine oxide] is similarly activated.

6) Structure and toxicity for insects of organic phosphorus compounds:

a) Structural alterations affect insect toxicity in much the same manner as they alter toxicity for higher 2231
animals. 2119

b) Generally speaking, the compounds of this class which are insecticidally effective are also toxic for 2231
mammals and diminution of toxicity for mammals reduces (though in some perhaps to a relatively lesser 854
degree) toxicity for insects. There are indications that in some cases, at least, in malathion for instance, 1123
the comparative safety of the potent insecticide for mammals is due (at least partly) to difficulties of absorption of the toxicant into the blood stream and nerve tissue.

7) Action of organic phosphorus insecticides and certain insecticide synergists:

a) Interest in the foregoing subject is attested by some recently published material indicative both of organic phosphorus insecticide potentiation by some so-called synergists as well as antagonism between one organic phosphate (malathion) and one synergist (piperonyl butoxide)

(1) Effect of certain synergists with some organic phosphorus insecticides; used as residues vs. DDT-R biotypes of *Musca domestica*: 1560

Synergist	% Mortality After 10 Min. Exposure To Residues Of						
	Malathion	EPN®	Methyl-parathion	Bayer 21/199	Bayer 21/200	Potasan®	Diazinon
	Ratio Synergist: Insecticide (mg/ft²)						
	5:25	1:10	1:10	5:25	5:25	5:25	1:10
NONE	3	22	51	20	4	18	23
N-Isobutyl undecyleneamide	70	98	97	87	6	100	75
Chrysanthemumic acid, α -propylpiperonyl ester	7	73	89	100	86	100	81
" , α -ethylpiperonyl "	7	90	84	100	64	100	59
" , α -isopropylpiperonyl ester	9	54	84	87	31	90	77
m-Dioxane, 5-butyl-5-ethyl-2-(3,4-methylene dioxyphenyl)	16	79	82	100	75	100	68
Piperonyl cyclonene	0	2	16	64	10	0	13
n-Octyl sulfoxide of isosafrole	0	58	87	97	86	94	94
Piperonyl butoxide	4	99	98	100	97	100	96
n-Propyl isome	0	6	3	76	36	30	32
Piperonylidene malonic acid, diethyl ester	3	53	58	80	49	71	—
Hexahydrophthalic acid, di-n-butyl ester	78	90	87	75	40	100	72
Phthalic acid, methyl-n-hexyl ester	56	96	97	98	70	90	—
N,N'-Diamylsuccinamic acid, propyl ester	35	90	95	82	57	88	—

(1) Effect of certain synergists with some organic phosphorus insecticides; used as residues vs. DDT-R biotypes of Musca domestica: 1560

Synergist	% Mortality After 10 Min. Exposure To Residues Of						
	Malathion	EPN®	Methyl-parathion	Bayer 21/199	Bayer 21/200	Potasan®	Diazinon
	Ratio Synergist: Insecticide (mg/ft^2)						
	5:25	1:10	1:10	5:25	5:25	5:25	1:10
N,N'-Dipropylsuccinamic acid, ethyl ester	67	99	68	88	26	88	–
N,N'-Diethylsuccinamic acid	19	18	27	45	0	53	–
N,N'-Diisopropylsuccinamic acid, ethyl ester	32	98	76	80	11	93	–
N,N'-Diethylglutaramic acid, ethyl ester	83	80	67	78	63	97	–
N,N'-Diisopropylglutaramic acid, methyl ester	65	97	95	93	69	82	–
N-(2-Ethylhexyl)bicycloheptene dicarboximide	33	92	88	88	67	89	–

(2) Duration of effectiveness (as residues) of organic phosphorus insecticides, and the same with synergists, vs. Musca domestica. 1560

Insecticide (mg/ft^2) And Synergist	Ratio Insecticide: Synergist	% Kill On Residues At Age (days) Shown			
		Initial	1 day	6 days	12 days
Malathion, S	1:0	18	5	4	0
" " + n-isobutyl undecyleneamide	1:10	97	94	94	80
" " + hexahydrophthalic acid, di-n-butylester	1:10	100	67	100	86
" " + N,N-diethylglutaramic acid, ethylester	1:10	100	27	27	88
Bayer 21/199, 2.5	1:0	17	5	0	0
" " + n-isobutylundecyleneamide	1:10	84	33	4	60
" " + piperonyl butoxide	1:10	100	100	100	100
" " + n-octylsulfoxide of isosafrole	1:10	100	83	100	96
" " + m-dioxane, 5-butyl-5-ethyl-2-(3,4 methylene dioxyphenyl)	1:10	100	100	100	100
EPN®, 1	1:0	2	0	0	0
" " + n-isobutylundecyleneamide	1:10	96	82	100	100
" " + piperonyl butoxide	1:10	94	93	33	35
" " "	1:2	100	100	91	16
Diazinon, 1	1:0	0	0	6	–
" " + n-isobutylundecyleneamide	1:10	70	55	25	–
" " + n-octylsulfoxide of isosafrole	1:10	89	80	94	–
" " + piperonyl butoxide	1:10	100	93	93	–

(3) Temperature and piperonyl butoxide effect on the action of malathion vs. DDT- non-R (KUN biotype) and DDT-R (Campus biotype) of Musca domestica: Topical application in acetone solution, mortality "readings" at 24 hrs. after treatment; 4 day old ♂ insects; ratio of piperonyl butoxide (PBO) to malathion = 10 to 1: 2575

Temperature (°F)	Campus Biotype				KUN Biotype			
	Malathion		Malathion + PBO		Malathion		Malathion + PBO	
	LD$_{50}$ µg/g	Slope	LD$_{50}$ (µg/g)	Slope	LD$_{50}$ (µg/g)	Slope	LD$_{50}$ (µg/g)	Slope
63	30.12 (26.85-33.65)	6.23	50.79 (38.02-62.81)	3.25	18.80 (18.39-20.53)	9.22	34.66 (30.89-45.58)	6.04
70	26.44 (22.34-27.33)	7.24	38.56 (34.44-45.55)	5.74	17.57 (13.81-17.62)	15.87	24.54 (23.52-28.11)	8.49
75	20.75 (19.41-21.63)	12.41	30.71 (27.38-34.28)	5.85	12.87 (11.93-13.43)	10.92	18.83 (16.7 -26.66)	3.15
82	19.56 (17.86-23.88)	4.48	34.66 (31.99-37.76)	7.93	13.39 (12.63-14.79)	8.26	19.43 (17.32-21.38)	7.62

ADDENDUM OF CERTAIN MOST RECENT DATA:

1) Organic phosphorus insecticides evaluated as toxicants for eggs and adults of Pediculus humanus corporis: 566
   a) Of 73 organic phosphorus compounds evaluated in cloth pad tests vs. laboratory colonies of Pediculus:
      (1) Parathion (in acetone solutions) proved the most effective ovicide, yielding complete kills at 0.0025%.
      (2) Sulfotepp (in acetone solutions) proved most effective against adult Pediculus, yielding complete kills at 0.0000025%.
      (3) Malathion and Chlorthion® (which hold some practical promise of use in louse powders because of low mammalian toxicity) proved completely effective vs. Pediculus adults, in acetone solutions at 0.001% and as acetone solutions vs. eggs at 0.05% and 1% respectively; in powder formulations vs. Pediculus eggs, these toxicants proved 97% effective at 0.5 and 1.0% respectively.
      (4) Pediculus adults and eggs from the DDT-R biotype showed no significant cross-resistance toward 10 organic phosphorus compounds.
      (5) Ovicidal effectiveness of malathion proved directly correlated with relative humidity.
      (6) Ovicidal effectiveness of Chlorthion® and malathion were directly correlated with the age of eggs.
      (7) Pyrophyllite base powders with 0.1% malathion or Chlorthion® proved completely effective vs. adult Pediculus for 14 days.

2) Organic phosphorus compounds vs. Myzus persicae on tobacco: 1307
   a) 1% parathion, 2.5% Metacide®, 5% malathion, 2.5% Chlorthion® and 5% diazinon dusts all yielded excellent control of heavy infestations.

MISCELLANEOUS EVALUATIONS OF TOXICITY FOR INSECTS OF CERTAIN OF THE MORE PROMINENT CONTEMPORARY ORGANIC PHOSPHORUS COMPOUNDS:

1) Toxicity for Anopheles quadrimaculatus (4th Instar, larva) in laboratory tests of certain organic phosphorus toxicants: 1766

Compound	% Mortality (48 Hours) At							
	0.1 ppm	0.05 ppm	0.025 ppm	0.01 ppm	0.005 ppm	0.0025 ppm	0.001 ppm	0.0005 ppm
Sulfotepp	100	———	———	———	———	———	74	34
Parathion	100	———	———	———	———	96	56	34
EPN®	100	———	———	———	———	96	32	—
Methyl parathion	100	———	———	———	———	67	—	—
O-(2-Chloro-4-nitrophenyl)-O,O-dimethyl thiophosphate	100	———	———	96	86	62	62	44
Malathion	100	———	96	80	80	60	40	24
Ethyl o-nitrophenyl thionobenzene phosphonate	100	———	———	———	70	80	4	—
Diazinon	100	———	———	———	36	20	—	—
Para-Oxon	100	———	———	82	50	—	—	—
O-(3-chloro-4-methylumbelliferone)-O,O-dimethyl thiophosphate	100	———	———	64	46	24	—	—
Chlorthion®	100	———	88	76	44	—	—	—
Potasan®	100	98	56	30	5	—	—	—
O,O-Diethyl O-piperonyl thiophosphate	100	94	58	26	—	—	—	—
NPD	94	—	62	30	—	—	—	—
DDT (for comparison)	—	—	—	100	94	49	24	—

2) Effectiveness of emulsions of organic phosphoric acid esters in field tests vs. larvae of Anopheles quadrimaculatus and Anopheles crucians:

Compounds	% Mortality (24 Hours) At							
	0.25 lbs/ acre	0.1 lbs/ acre	0.05 lbs/ acre	0.025 lbs/ acre	0.01 lbs/ acre	0.005 lbs/ acre	0.0025 lbs/ acre	0.001 lbs/ acre
EPN®	—	—	95	96	96	95	92	91
O-(3-chloro-4-methylumbelliferone)-O,O-dimethyl thiophosphate	—	—	98	98	99	96	91	84
Parathion	—	—	97	97	92	99	88	—
Methyl Parathion	—	100	98	83	69	51	50	—
Ethyl o-nitrophenyl thionobenzene phosphate	—	99	80	88	75	70	69	71
Chlorthion®	100	99	82	73	57	50	—	—
Diazinon	—	97	97	79	58	65	55	53
O-(2-Chloro-4-nitrophenyl)-O,O-dimethyl thiophosphate	—	99	72	78	49	30	—	—
NPD	100	97	84	87	79	—	—	—
Para-Oxon	—	90	77	54	46	45	49	31
Sulfotepp	—	85	72	73	63	53	30	—
Malathion	90	78	79	68	60	—	—	—
O,O-Diethyl O-piperonyl thiophosphate	—	—	78	64	75	74	45	35
Potasan®	—	77	59	72	52	—	—	—
DDT (for comparison)	—	—	99	98	99	98	95	92

3) Toxicity of certain organic phosphorus compounds for the overwintering eggs of Aphis pomi and Operophtera brumata, tested by 10 second immersion of 100 to >300 eggs per trial: 899

Compound	% Mortality At Concentration (%)			
	0.2%	0.05%	0.2%	0.05%
	A. pomi		O. brumate	
Triethyl phosphate	1.4	0	3.1	7.1
Triphenyl phosphate	14.1	0	8.0	6.4
Tri-o-tolyl phosphate	0	7.1	5.8	7.9
Triphenyl phosphine	13.9	5.1	3.4	3.6
HETP	7.4	1.1	6.2	3.7
p-Nitrophenyl diethyl thionophosphate	100	78.6	95.4	90.8
Diethyl acetyl phosphate	5.7	8.4	8.7	1.3
p-Nitrophenyl diethyl phosphate	99.6	100	7.8	4.4
Diphenyl ethyl thionophosphate	0	8.1	8.5	4.8
p-Nitrophenyl dichlorothionophosphonite	40.4	10.3	—	10.2
Diphenyl chlorothionophosphonate	25.9	4.9	4.0	3.0
Tri-(p-nitrophenyl) thionophosphate	5.3	0.6	1.9	4.3

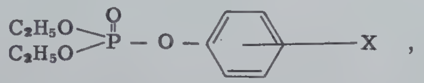
3) Toxicity of certain organic phosphorus compounds for the overwintering eggs of Aphis pomi and Operophtera brumata, tested by 10 second immersion of 100 to >300 eggs per trial: 899

Compound	% Mortality At Concentration (%)			
	0.2%	0.05%	0.2%	0.05%
	A. pomi		O. brumata	
Tri-(p-chlorophenyl) thionophosphate	15.7	13.0	1.6	1.9
TEPP	3.3	2.6	7.2	6.5
Diethyl-1-carbethoxyprop-1-en-2-yl phosphate	100	86.3	18.3	2.3
Phenyl diethyl phosphate	59.3	2.9	2.5	3.3
p-Chlorophenyl diethyl phosphate	93.9	14.6	2.5	2.2
Phenyl diethyl thionophosphate	39.9	3.7	1.7	1.6
Triphenyl thionophosphate	19.0	23.7	0	3.7
Tetraethyl dithionopyrophosphate	100	54.6	24.0	4.6
Tetraethyl monothiono pyrophosphate	12.0	2.4	19.0	1.6
Pyrophosphoric tetrakis dimethylamide	9.0	0	1.4	0
Control (% hatch)	69.9		97.1	

ADDENDUM OF RECENT PUBLISHED DATA ON ORGANIC PHOSPHATES:

1) Diethyl substituted phenyl phosphates; structure and insecticidal activity; Fukuto, T.R., and Metcalf, R. L., Journal of Food and Agricultural Chemistry 4(11): 930, 1956*:

a) A consideration of the insecticidal action of a series of compounds of the general structure



with substitution either at the meta-or para-position.

b) Evaluation based on LD_{50}, with analysis of the correlation of toxicity with choline esterase(s) inhibition activity of the compounds. The following premises are taken as valid:

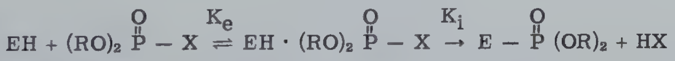
(1) Toxicity to insects and mammals of the "organophosphorus" insecticides depends on the biochemical processes of the animal and physicochemical properties of the toxicant.

(2) Fundamentally, there is agreement that toxicity of "organophosphorus" toxicants for mammals is associated with inhibition of choline esterase(s), although other enzymes, viz., liver esterase, chymotrypsin, trypsin are also inhibited in vitro.

(3) Recent evidence tends to support the view that toxicity for insects of "organophosphorus" compounds is also associated with the choline esterase(s) enzyme system(s).

(4) Reaction between "organophosphorus" toxicant and enzyme(s) yields enzyme inhibition by irreversible phosphorylation at some active site of the enzyme by the toxicant, models being provided by para-oxon and DFP inhibitions of chymotrypsin, resulting from an equimolar reaction of toxicant with enzyme to give inactive phosphorylated chymotrypsin.

(5) Inhibition of erythrocyte ChE by paraoxon (and analogues) is kinetically of the first order and bimolecular, the rate constants being generally parallel to rate of hydrolysis in water. The mechanism proposed:



$$EH + (RO)_2\overset{O}{\overset{\|}{P}} - X \overset{K_e}{\rightleftharpoons} EH \cdot (RO)_2\overset{O}{\overset{\|}{P}} - X \xrightarrow{K_i} E - \overset{O}{\overset{\|}{P}}(OR)_2 + HX$$

where EH = enzyme, R = short chain alkyl group, X = any displaceable group (halogen, alkoxy, aryloxy), the enzyme inhibiting ability of the "organophosphate" being related directly to P – X bond lability.

c) The compounds under consideration lend themselves to this study because of direct relation between substituent(s) on the benzene nucleus and reactivity of the phosphorus - oxygen bond. Hammett's equation furnishes a quantitative relationship for m- and p-substituents:

$$\log k/k_0 = \rho\sigma$$

(1) The compounds tested (among others for which see below) physical constants:

Diethyl Substituted Phenyl Phosphate	P. (°C) At 0.05 mmHg.	$n_D^{25°}$
m - Nitro	140 (at 0.1 mmHg)	1.4972
p - Cyano	103	1.4920
m - tert-Butyl	110	1.4770
m - Methoxy	114-118	1.4842
p - Methoxy	114	1.4861
p - Methylmercapto	131-133	1.5254
p - Methylsulfinyl	165	1.5146
p - Methylsulfonyl	185	1.5028
p - Formyl	130	1.5002
m - Dimethylamino	135	1.5100

*Attention was drawn to these data too late to permit inclusion of the source in the alphabetic cumulative bibliography of this work.

(2) Biological activity of Diethyl substituted phenyl phosphates:

Compound	ID_{50} For Fly Brain ChE	LD_{50} (S.D. = ± 30%) For		
		Musca domestica (μg/g)	Heliothrips haemorrhoidalis (% Conc.)	Metatetranychus citri (% Conc.)
2,4-di NO_2	3.0×10^{-9} M	155	0.01	0.01
p-NO_2	2.6×10^{-8} M	0.5	.0001	.001
o-NO_2	5×10^{-8} M	7.0	.001	.003
m-NO_2	5.0×10^{-8} M	9.8	.005	.03
2,4,5-tri-Cl	6.0×10^{-9} M	8.0	.03	.0003
2,4,6-tri-Cl	3.3×10^{-6} M	175	.03	.03
2,4-di-Cl	5.0×10^{-7} M	15.0	.003	.1
o-Cl	2.0×10^{-5} M	250	.01	> .1
p-Cl	3.0×10^{-5} M	150	.01	> .1
p-$\overset{+}{S}(CH_3)_2CH_3SO_4^-$	3.4×10^{-9} M	17.5	.0002	.001
p-SO_2CH_3	2.5×10^{-7} M	2.5	.0001	.001
p-$SOCH_3$	3.1×10^{-6} M	1.5	.0001	.0008
p-SCH_3	3.3×10^{-5} M	2.0	.0001	.0002
m-$\overset{+}{N}(CH_3)_3I^-$	3.0×10^{-8} M	>500	> .1	> .1
m-$N(CH_3)_2$	4.0×10^{-7} M	25	.1	.1
p-CN	1.3×10^{-7} M	3.5	.00002	.002
m-OCH_3	1.3×10^{-4} M	>500	.02	.3
p-OCH_3	$>1.0 \times 10^{-3}$ M	>500	1.0	1.0
m-tert,-butyl	9.0×10^{-7} M	500	.003	.1
p-tert-butyl	1.0×10^{-4} M	>500	.1	> .1
p-CH_3	$>1.0 \times 10^{-3}$ M	>500	> .1	> .1
H	$>1.0 \times 10^{-3}$ M	>500	> .1	> .1
p-CHO	1.5×10^{-7} M	>500	.05	.05
p-COOH	8.5×10^{-7} M	150	.005	.01

(a) Degree of inhibition of ChE appears as a direct function of electron-withdrawing capacity of the substituents on the benzene nucleus. The relationship is borne out by a plot of -log ID_{50} values vs. Hammett's sigma (σ) constants for the substituents. In general the points are dispersed on a straight line with -log ID_{50} increasing with increase in sigma values.

(b) Hammett's equation applies to p- and m- substituents only; o-nitrophenyl, 2,4-dinitrophenyl, 2,4,5-trichlorophenyl etc., substituted compounds show that the effect of 2 or more substituents is additive.

(c) Steric hindrance plays a part; consider, for example, the difference between 2,4,5-tri-Cl and 2,4,6-tri-Cl. The chlorines at 2 and 6 slow the reaction of phosphate with ChE.

(3) Frequency (Cm^{-1}) of Phosphorus-Oxygen-Aromatic stretching vibrations of various diethyl substituted phenyl phosphates:

Compound	Wave Number (cm^{-1})
m - Methoxyphenyl	1200
p - "	1205
m - tert.-butylphenyl	1207
Phenyl	1215
p - Chlorophenyl	1217
p - Methylmercaptophenyl	1218
p - Methylphenyl	1219
p - Methylsulfinylphenyl	1223
p - Methylsulfonylphenyl	1226
p - Carboxyphenyl	1227
p - Formylphenyl	1229
m - Nitrophenyl	1230
p - Nitrophenyl	1240
p - Cyanophenyl	1241
2,4,5-Trichlorophenyl	1253
2,4-Dinitrophenyl	1265

(a) Wave number is a function of electron-donating or attracting property of the substituent and a measure of P — O bond reactivity.

(b) Plot of -log ID_{50} for Musca brain ChE against frequency is similar to the plot against Hammett's sigma values - the wave frequency and -log ID_{50} increasing together in a roughly straight line point distribution.

(4) First order hydrolysis constants of diethyl substituted phenyl phosphates in 0.1M diethyl barbituric acid (pH 9.5):

(4) First order hydrolysis constants of diethyl substituted phenyl phosphates in 0.1M diethyl barbituric acid (pH 9.5):

Substituted Phosphate	$K_{hyd.}$ Min^{-1}
Phenyl	9.2×10^{-6}
m-tert.-Butylphenyl	8.6×10^{-6}
m-Dimethylaminophenyl	1.9×10^{-6}
p-Chlorophenyl	3.2×10^{-5}
o-Chlorophenyl	5.1×10^{-5}
2,4,5-Trichlorophenyl	7.9×10^{-5}
2,4-Dichlorophenyl	4.8×10^{-5}
m-Methoxyphenyl	8.9×10^{-6}
p-Nitrophenyl	2.7×10^{-4}
m-Nitrophenyl	9.8×10^{-5}
2,4-Dinitrophenyl	5.7×10^{-3}

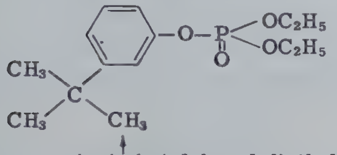
(a) A plot of log K_{hyd} against Hammett's sigma shows the mono-substituted phenyl phosphates to conform to Hammett's equation.

2) Summary:

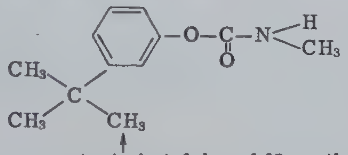
a) Choline esterase inhibition, hydrolysis constants, Hammett's sigma constants, and P — O — aromatic stretching frequencies show inter-relationship.

(1) Sigma values, readily gotten from experience data and infra-red measurements, have value in predicting ChE inhibiting ability of compounds of the type considered.

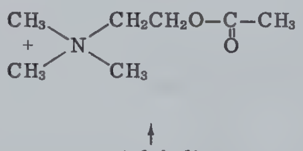
b) There are exceptions: m-Dimethylaminophenyl and m-tert.-butylphenyl diethyl phosphates are greatly more inhibitory than Hammett's treatment would predict. The influence of m-dimethylamino- and m-tert.-butyl-groups on activity is shown also with substituted phenyl-N-carbamates. It is suggested that m-dimethylaminophenyl- and m-tert.-butylphenyl-diethyl phosphates inhibit ChE by competition rather than irreversible phosphorylation. Note the following similarities:



m-tert.-butylphenyl diethylphosphate



m-tert.-butylphenyl N-methylcarbamate



acetylcholine

c) The nature of the insect plays a role. Penetration of toxicant through the insect cuticle and lipoid nerve sheath is a factor in toxicity. Polar compounds are poor in this regard. Consider the low toxicity of diethyl-m-dimethylaminophenyl phosphate methiodide and diethyl p-methyl mercaptophenyl phosphate methosulfate.

d) Chemical or metabolic fate in the insect influences the toxic potency of the toxicant. High activity of p-methylmercaptophenyl- and p-methylsulfinylphenyl-diethyl phosphate may be due to oxidation to the sulfone in the insect.

e) Diethyl p-cyanophenyl phosphate and diethyl p-methylmercaptophenyl phosphate (and its sulfoxide and sulfone oxidation products) are of high effectiveness insecticidally, in direct line with the prediction of such activity by high Hammett's sigma values.

f) While the schema of inhibition suggested at 1) b) (5) in this treatment appears to hold (with the enzyme-inhibitor complex as a transitional state in nucleophilic x moiety displacement on the P atom in case of irreversible phosphorylation) there are evidences that reversible inhibition with some phosphates may occur.

(1) Both irreversible and reversible inhibition may be at work in certain cases depending on K_e and K_i values.

(2) Some compounds (which spatially resemble acetyl choline closely) with relatively labile P — X bonds show K_e values which favor complex formation—a condition which should enhance the total inhibition of ChE. Examples are: O,O-Diethyl S-2-diethylaminoethyl phosphorothiolate oxalate, 3-(diethoxyphosphinyloxy)-N-methylquinolinium methyl sulfate, O,O-diethyl S-2-ethyl mercaptoethyl phosphorothiolate methosulfate.

(3) In case of m-dimethylaminophenyl diethyl phosphate and m-tert.-butylphenyldiethyl phosphate K_e approaches optimum and k_i is very small. For these substances competitive inhibition is apparently the paramount toxic action.

135

ORGANIC THIOCYANATES; THIOCYANOACETATES

GENERAL [Refs.: 314,353,2226,1059,757,2815,2231,2331,311,414,2533,413,1801,1236,1430,2219,2816,1958, 851,2221]

The toxicants which may be grouped under the general category of organic thiocyanates and thiocyanoacetates, several of which are in wide use under the common designation Lethane®, for example Lethane 384®, Lethane 60® etc., are notable for yielding a rapid paralysis ("knockdown" ["KD"]) of insects. In consequence, these compounds have found use in various household type sprays to control flies, mosquitoes, cockroaches, etc., and as sprays for domestic animals and livestock to control lice etc. Some possess high fumigant activity and others are of value to control aphids (being highly toxic to adults, nymphs, eggs) and against such greenhouse and field insects as mealy bugs, thrips, white fly and leaf hoppers. The useful toxicity of this group of compounds for insects must be balanced against a rather high phytotoxic hazard, just as their ability to kill flies and other household insects must be considered in conjuction with the highly irritant quality of some of them. Also, the thiocyanates tend to have unpleasant odors which limit their use in household sprays, a disadvantage which is considerably less among the thiocyanoacetates. Among the commonly employed substances belonging to this group of toxicants are lauryl thiocyanate (Loro®), isobornyl thiocyanoacetate (Thanite®), β-butoxy-β'-thiocyanodiethyl ether (Lethane 384®), β-thiocyanoethyl laurate (Lethane 60®), β,β'-dithiocyanodiethyl ether (Lethane A-70®), Lethane Special (a 3:1 mixture of Lethane 60® and Lethane 384®). A treatment in detail of each of these substances may be consulted in the present work.

CHEMICAL STRUCTURE AND INSECTICIDAL ACTION:

1) The aliphatic (alkyl) thiocyanates (isothiocyanates) are most used as contact insecticides and as fumigants. Contact activity tends to be at maximum in the carbon chain length range of C_8 to C_{14}, depending on the insect species. Within this range, activity is generally at its highest at C_{10} or C_{12} with compounds of carbon chain length lower or higher showing less contact activity. Fumigant activity is highest in the lower members, for instance methyl thiocyanate, and even here a boiling point of 116°C is probably somewhat high for a practical fumigant. 311

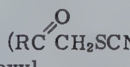
2) Aromatic (aryl) thiocyanates have been less studied as insecticides. However, α-naphthyl isothiocyanate has been used in commercial fly-sprays. Acenaphthylene thiocyanate is entirely non-toxic to Sitophilus granarius for which the LC_{50} (at 25°C; 5 hrs. exposure) of methyl thiocyanate is 3.5 mg/l, LC_{99} 5.7 mg/l. 311 2816 2999

3) The "knockdown" activity of alkyl thiocyanates is relatively low. High "knockdown" action is conferred by linkage of the thiocyano-radical through a keto-methylene group to a lipoid-soluble hydrocarbon residue to yield substances of the general nature of $R \cdot CO \cdot CH_2 \cdot SCN$ and $R \cdot O \cdot CO \cdot CH_2 \cdot SCN$, which are the most active α-thiocyanoketones and thiocyanoacetates in terms of "knockdown." They tend, however, to be too irritant to eyes and nose for domestic fly spray use. A compromise is reached by employing thiocyanoacetates derived from C_{10} saturated alcohols, which possess moderately high "knockdown" and are non-irritant as well as highly toxic for insects. 1236

4) The replacement of -SCN by -OH, a halogen, or -NCS yields loss of insecticidal activity. 1236

5) Aliphatic thiocyanate toxicity for Musca is enhanced by adding an ω-hydroxyl group, but this lessens stability and confers unpleasant smell. Esterification (with lower aliphatic acids) of the hydroxyl of thiocyanohydrin yields stable esters of high "KD" activity such as $C_2H_5COO(CH_2)_4SCN$, $C_2H_5COO(CH_2)_2SCN$ and $n\text{-}C_3H_7COO(CH_2)_3SCN$. 1304

6) Thiocyanoacetates with the group $-OCOCH_2SCN$, although less noxious in smell than thiocyanates, are more irritant than the latter for mammals, while being very toxic for insects with a high "KD" potency. 1236 2937

7) α-Thiocyanoketones ( $R\overset{O}{\overset{\|}{C}}CH_2SCN$) are more toxic than thiocyanoacetates, $ROCCH_2SCN$ (for Musca) activity being highest at n-hexyl. 1236 2937

8) Comparative toxicity of some thiocyanates and thiocyanoacetates for several insect species: 414,413 311,1236

Compound	LC_{50} *M. sanborni (Contact Spray)	LC_{50} (% Conc.) (Direct Spray) Pediculus humanus	LC_{50} (% Conc.) (Direct Spray) Cimex lectularius	KD_{50} (Minutes) For Musca domestica
n-Hexyl thiocyanate	1:1200	–	–	–
n-Octyl "	1:2500	5	–	–
n-Decyl "	1:2800	5	–	–

*Macrosiphoniella sanborni.

8) Comparative toxicity of some thiocyanates and thiocyanoacetates for several insect species: 414,413 311,1236

Compound	LC_{50} *M. sanborni (Contact Spray)	LC_{50} (% Conc.) (Direct Spray) Pediculus humanus	Cimex lectularius	KD_{50} (Minutes) For Musca domestica
n-Dodecyl thiocyanate (lauryl)	1:3000	5	—	—
n-Tetradecyl " (myristyl)	1:2700	11	—	—
n-Hexadecyl " (cetyl)	1:1700	18	—	—
n-Octadecyl "	—	25	—	—
Methyl thiocyanoacetate	—	—	—	10
n-Hexyl "	—	—	—	5
2-Ethylhexyl "	—	—	—	7.5
Capryl "	—	—	—	10
Lauryl "	—	—	—	10 (2% "KD" in 10 minutes)
Lethane 384®	—	1.5 { LD_{50} .27 μg/insect 135 μg/g }	4.0 { LD_{50} 1.8 μg/insect 450 μg/g }	—
Lethane 60®	—	8.1	32.0	—
Lethane Special®	—	2.5	12.5	—
Lauryl thiocyanate	—	6.0	19.5	—
Isobornyl thiocyanoacetate	—	3.2	75.0	—

*Macrosiphoniella sanborni.

9) Methyl thiocyanate; fumigant toxicity at 25°C, 5 hrs. exposure, empty vessel method. 2816

			Ethyl thioacetate	
Tribolium confusum	LC_{50} 1.6 mg/l	LC_{99} 2.6 mg/l	LC_{50} 45 mg/l	LC_{99} 63 mg/l
Sitophilus granarius	LC_{50} 3.5 mg/l	LC_{99} 5.7 mg/l	LC_{50} 20 mg/l	LC_{99} 34 mg/l

10) Toxicity of thiocyanogen compounds for Aphis rumicis as contact sprays in aqueous solution at 0.1% concentration (with spreader Penetrol or Tanoyl:) 1430

Compound	% Mortality (Duplicate Tests With Toxicant + Spreader	Spreader Alone
n-Butyl thiocyanate	33.3;31.0	23.1;22.5
Phenyl thiocyanate	24.5;23.4	16.3;20.8
Methyl thiocyanate	64.3;43.2	23.5;18.0
Methyl thiocyanoacetate	66.0;54.7	28.5;35.2
Ethyl β-thiocyanopropionate	53.0;46.2	—
γ-Thiocyanopropyl phenyl ether*	98.0;93.7	28.8;22.2
γ-Bromopropyl phenyl ether	25.3;34.3	—
2-Thiocyanooctane	37.3;52.8	25.3;13.9
β-Thiocyanoethyl ethyl ether	71.0;71.0	47.2;34.3
β-Thiocyanoethyl methyl ether	86.7;86.5	16.2;21.3
p-Thiocyanoaniline	99.2;99.1	24.1;28.6
Benzyl thiocyanate	91.7;81.6	20.0;26.9
Thiocyanomethyl phenyl ketone	65.0;69.4	42.8;47.3
β-Thiocyanoacetate of diethyleneglycolmonobutyl ether	92.9;93.4	43.3;42.6
β-Thiocyanoethyl phenyl ether	93.6;94.5	43.8;45.8

*At 0.1% in water + 0.5% penetrol gave 98% mortality of Pseudococcus citri (on Coleus) and 100% mortality of Tetranychus telarius (on Rosa) with no plant injury to nasturtium, petunia, English ivy, egg-plant, balsam, Jerusalem cherry, cabbage, potato, peach, club moss, Geranium, gladiolus, marigold, Cosmos, Salvia, heliotrope, cotton, but with injury to buckwheat.

11) Toxicity of certain thiocyanates and thiocyanoacetates for several insect species: 2219

Compound	Insect	Route	Amount (μg/g) To Yield Mortality Indicated 0%	50%	100%
Lethane 384® *	Periplaneta americana	Topical	♂360;♀560	♂660;♀1260	♂1360;2300
"	"	Injection	♂100;♀120	♂150;♀ 200	♂ 200;♀400
"	Oncopeltus fasciatus	Topical	120	400	750
"	Popillia japonica	Topical	350	800	1700
"	"	Injection	100	300	900
"	Tenebrio molitor	Topical	400	850	1600
Thanite® **	Periplaneta americana	Topical	♂3500;♀>7000	♂4800	♂ca6000
"	"	Injection	♂♀200	♂♀300	♂♀450
Loro® ***	"	Injection	♂♀400	♂♀900	♂♀1500

*50% β-butoxy-β'-thiocyanodiethyl ether.
**Terpinyl thiocyanoacetate.
***Lauryl thiocyanate 60% (93% total mixed thiocyanates).

12) Thiocyanoacetates: "Knockdown" activity for Musca domestica; irritation action for mammals; tests conducted with 1.0% w/w concentrations in a chamber 2 x 2 x 4½ ft, 80 - 100 flies per test; values = means of 3 tests; used as space sprays; items with*, e.g., Methyl* are followed by thiocyanoacetate: 1236

Thiocyanoacetate	% Knockdown In				Irritation For Mammals (Eyes, Skin, Mucosae)
	2.5 min.	5 min.	7.5 min.	10 min.	
Methyl*	2	15	37	58	Irritant
n-Hexyl*	9	56	99	100	Irritant
Cyclohexyl*	26	47	76	99	Irritant
2-Ethylhexyl*	14	42	56	84	Slightly irritant
Capryl*	0	9	23	58	Slightly irritant
Carvomenthyl*	3	48	64	91	Non-irritant
Isobornyl* (Thanite®)	14	42	65	93	Non-irritant
Fenchyl*	7	35	59	95	Non-irritant
Decahydro-2-naphthyl*	7	19	32	51	Non-irritant
1-Methyl-3-cyclohexyl-n-propyl*	2	13	21	60	Non-irritant
4-Tert.-butyl-cyclohexyl*	1	10	23	78	Non-irritant
"	5	18	27	51	Non-irritant
Lauryl*	0	0	0	2	Non-irritant
4-(α,α,β,γ-tetramethyl-n-butyl)phenyl*	6	15	15	16	Non-irritant
Tetrahydrofurfuryl*	0	17	23	25	Very irritant
1-Methyl-3-(α-tetrahydrofuryl)-n-propyl*	2	42	61	91	Very irritant
β,β'-Di-(α-tetrahydrofuryl)-diethyl carbinyl*	0	1	6	28	Very irritant
2-Methoxyethyl*	14	16	27	35	Irritant
2-Butoxyethyl*	4	32	53	86	Irritant
2-Caproxyethyl*	5	35	49	88	Slightly irritant
2-Fenchoxyethyl*	23	46	73	90	Non-irritant
2-(1-Methyl-3-(α-tetrahydrofuryl)-n-propoxyethyl)*	40	61	78	93	Very irritant
2-β-Naphthoxyethyl*	0	0	0	5	Irritant
2-(2-Ethoxyethoxy) ethyl*	6	12	12	14	Slightly irritant
Thiocyanoacetone	25	41	69	91	Very irritant
Thiocyano-4-cyclohexyl butanone-(2)	1	23	61	90	Irritant
Thiocyanotetrahydroionone	0	0	0	4	Non-irritant
Phenyl*	1	6	24	36	Irritant
α-Naphthyl*	0	5	7	14	Irritant
4-(α,α,β,γ-Tetramethyl)-n-butylphenyl*	0	0	0	0	Irritant
ω-Thiocyanoacetophenone	49	74	82	98	Very irritant
ω-Thiocyano-4-methoxyacetophenone	0	2	2	3	Very irritant
2-Thiocyanocyclohexanone	21	40	47	57	Irritant
2-Thiocyano-4-tert.-butyl-cyclohexanone	0	0	0	6	Irritant
1-Thiocyanoheptene-(1)	2	4	4	7	Non-irritant
5-Thiocyano-2:3-dihydropyran	1	3	3	3	Non-irritant
Ethyl thiocyanofumarate	1	1	1	2	Non-irritant
4-Methyl-2-hydroxythiazole	1	1	1	2	Non-irritant
4-Phenyl-2-hydroxythiazole	1	2	2	3	Non-irritant
Acetone control	0	1	1	1	—
Kerosene control	0	0	0	0	—

variation (with concentration) of "Knockdown" and irritation for mammals: 1236

Compound	Concentration (%, w/w)	% "Knockdown" In				Irritation
		2.5 min.	5 min.	7.5 min.	10 min.	
Carvomenthyl thiocyanoacetate	1	12	30	58	79	Slightly irritant
"	2	24	50	76	100	Moderately irritant
"	4	46	64	78	97	Irritant
Decahydro-2-naphthyl thiocyanoacetate	1	7	19	32	51	Non-irritant
"	2	29	46	60	95	Slightly irritant
"	4	29	59	80	98	Irritant
4-tert.-Butylcyclohexyl thiocyanoacetate	1	5	18	27	51	Non-irritant
"	2	15	35	55	93	Irritant
"	4	13	52	63	97	Irritant
" (purified)	1	0	9	37	65	Non-irritant
" "	2	16	48	62	92	Slightly irritant
Isobornyl thiocyanoacetate (Thanite®)	1	8	34	52	75	Non-irritant
"	2	23	56	69	96	Slightly irritant
"	4	37	64	77	98	Irritant

13) Thiocyanates which have been tested as fumigants against Limonius canus and Limonius californicus in 5 hrs. exposures, at 77°F, in soil: 1958

Compound	LC_{50} (mg/l) For Limonius canus And L. californicus
Allyl isothiocyanate	2.33
Ethyl isothiocyanate	3.2
Isopropyl thiocyanate	228.8
Ethyl thiocyanate	297.8

14) Toxicity of some insecticidally employed thiocyanates and thiocyanoacetates for mammals: 1951,1952 2078,2506

Compound	Animal	Route	LD_{50}	Remarks
Isobornyl thiocyanoacetate	Rat	or	1000 mg/k	Single acute dose.
"	Rat	or	6 cc/k	".
"	Guinea Pig	or	2 cc/k	".
"	Rabbit	ct	6.0 cc/k	Single acute application.
β-Thiocyanoethyl laurate	Rat	or	500 mg/k	Single acute dose.
"	Rat	or	0.7 cc/k	".
"	Rat	ip	0.16 cc/k	".
"	Rat	sc	0.5 cc/k	".
"	Guinea Pig	or	0.75 cc/k	".
"	Guinea Pig	ip	0.13 cc/k	".
"	Guinea Pig	sc	0.7 cc/k	".
"	Rabbit	or	0.2 cc/k	".
"	Rabbit	ip	0.125 cc/k	".
"	Rabbit	sc	0.25 cc/k	".
"	Rabbit	ct	5.0 cc/k	".
"	Dog	or	0.25 cc/k	".
"	Dog	sc	0.625 cc/k	".
β-Butoxy-β'-thiocyanodiethyl ether	Rat	or	90 mg/k	Single acute dose.
"	Rat	or	0.25 cc/k	".
"	Rat	ip	0.045 cc/k	".
"	Rat	sc	0.275 cc/k	".
"	Guinea Pig	or	0.2 cc/k	".
"	Guinea Pig	ip	0.042 cc/k	".
"	Guinea Pig	sc	0.225 cc/k	".
"	Rabbit	or	0.06 cc/k	".
"	Rabbit	ip	0.04 cc/k	".
"	Rabbit	sc	0.05 cc/k	".
"	Rabbit	ct	0.125-0.25 cc/k	Single acute application.
"	Dog	or	0.25 cc/k	Single acute dose.
"	Dog	sc	0.625 cc/k	".
β-Thiocyanoethyl laurate	Dog	inhalation at 1 hr/day for 15 days, 1% and 5% concentrations: Survived; death at concentrations >5%.		
"	Guinea Pigs	inhalation; sprayed 3 hrs/day with 1% concentration: Survived.		414

a) The lower thiocyanates are especially toxic for mammals; use of dodecyl (lauryl) thiocyanate in fly sprays represents a compromise between a relatively high toxicity for the insect and safety for man at insecticidal dosages.

b) Isobornyl thiocyanoacetate is rather more irritant for man than the various Lethanes® and Loro® and should not be permitted to reach the eyes or other mucous membranes if used against body or head lice or as a spray on the bodies of domestic animals, livestock or poultry. 851

c) The pharmacological, pharmacodynamic, physiological, and other aspects of the action of thiocyanates (chiefly inorganic forms such as sodium and potassium thiocyanates) are succinctly discussed in Ref. 851. Particular attention is given to hypotensive action and direct effects upon cellular activity.

d) Symptoms of intoxication in mammals in organic thiocyanate poisoning include: Restlessness, severe depression, dyspnea, cyanosis, convulsions (tonic) and death in respiratory paralysis. Death is swift upon intake of a lethal dose. Pathology includes: Hepatic vacuolization (parenchyma cells) and, in the pulmonary tree, a pneumonitis of monocytic fibrinous nature. 1951 2078

(1) Liberation of HCN from alkyl thiocyanates has been claimed by some as a mechanism of poisoning. The liberation of HCN from methyl and ethyl thiocyanates and, to a lesser extent, from β'-thiocyanodiethyl ether (but not from lauryl thiocyanate) by liver breis in vitro has been reported. 3201

(2) Liberation of CN^- in the bloodstream of rabbits intoxicated with tetramethylene thiocyanohydrin has been reported and in cats this compound raised the blood pressure of animals under artificial respiration indicating a possible cyanide-like action on internal respiration. p-Aminopropiophenone protects rabbits against lethal doses of tetramethylene thiocyanate thus supporting the premise of a CN^--like action. 1304

- (3) An oxidase (oxidizing thiocyanate to cyanide) has been reported in mammalian erythrocytes (man, rat, rabbit, dog). 1214
- (4) Action of the thiocyanoacetates and thiocyanoketones on an enzyme system with special affinity for $-COCH_2SCN$ has been postulated by some. 1236

MODE OF ACTION, PHARMACODYNAMICS ETC., IN INSECTS:

- a) The rapid paralytic ("knockdown") action of these compounds on insects has suggested an essential neurotoxic action on the cellular plane. 2600
    - (1) In Periplaneta americana, Culex pipiens and Aëdes aegypti following treatment with Thanite® (isobornyl thiocyanoacetate) selective nerve tissue degeneration with lesions (vacuolization) similar to those induced by pyrethrins, although not so marked, have been reported. Larvae of mosquitoes revealed these lesions while still capable of feeble movement, a fact taken to preclude the possibility of a post-mortem artifact.
    - (2) In Tenebrio molitor larvae topical application of γ-thiocyanopropyl phenyl ether resulted in cellular tigrolysis and tissue vacuolization in the central nerve cord. The effect was pyrethrin-like, but to a lesser degree than in pyrethrin poisoning. 1430
    - (3) In β-butoxy-β'-thiocyanodiethyl ether and isobornyl thiocyanoacetate treated Musca domestica (prepared in the moribund state for histological examination) degeneration of nerve cell structure has been reported, namely: Pycnotic nuclei and dissolution of cytoplasmic fine structures. In muscle tissue nuclear pycnosis and destruction of the nuclear membrane was noted. Others have suggested that these effects are general post-mortem artifacts. 1422
- b) In the isolated heart of Blatta orientalis certain aliphatic thiocyanates brought about a general decline of the contraction rate (even to cessation of beat) and increase in heart dilation. 3382
    - (1) Methyl- and ethyl- thiocyanates proved least effective; isopropyl-, n-propyl-, butyl- thiocyanates yielded intermediate effects; trimethylene thiocyanate, butyl carbitol thiocyanate, β,β'-Dithiocyanodiethyl ether, diethylene glycol thiocyanate and diethylene glycol dithiocyanoacetate proved most effective. At 0.006% these last produced rapid heart-rate decline with final cessation of beat.
- c) Topical treatments (measured drop on abdomen) of Periplaneta americana with a number of thiocyanates revealed γ-thiocyanopropylphenyl ether to be the most toxic by contact. 1430
    - (1) A sequence of symptoms was produced: Irritation at site of application within 15 minutes; longitudinal convulsive twitching, with partial paralysis of last leg pair; complete paralysis of legs within 1 hour not excluding, however, twitches at 1 per second with the insect incapable of walking; gradual diminution of convulsions until death in ca. 3 hrs.
- d) The effects of β-butoxy-β'-thiocyanodiethyl ether on the insect heart and circulation (Periplaneta) have suggested to some an HCN-like action in insects. An action as poisons of cellular respiratory systems is postulated for organic thiocyanates and related compounds. 588
    - (1) Lethane 60® and Lethane 384® have shown marked inhibition at 10^{-3} M of Periplaneta americana coxal muscle cytochrome oxidase systems in vitro, as measured by O_2 uptake in Warburg's apparatus. 2305
- e) Explanations of the mode of action of toxicants of this group on the basis of their ability to penetrate the insect cuticula have been advanced relating toxicity to carbon-chain length of the alkyl component. 1236,311 2123,983
- f) Spraying of Tribolium castaneum adults with lauryl thiocyanate in an aqueous contact spray under various conditions of temperature before and after treatment has yielded the following results: 2532

Holding Temperature Of Insects Before Treatment	LC_{50} (% v/v) Under Various Post-treatment Holding Conditions		
	Cold	Hot	Mean
Cold (56°-59°F, R.H. 50%)	0.172	0.231 →	0.199
Hot (80.6°F, R.H. 52%)	0.153	0.247 →	0.195
	(Mean) 0.163	(Mean) 0.239 →	0.197

These results suggest a generally negative temperature coefficient of action.

136

OVIPOSITION INHIBITORS FOR MUSCA DOMESTICA

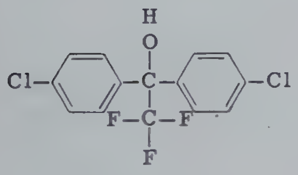
N.B. The data in this section derive wholly from the following source: Ascher, K.R.S., Science 125(3254): 938, 1957, a paper seen too late for inclusion in the cumulative, alphabetic bibliography of this work. The bibliography in support of the source given is reproduced at the end of this section.

GENERAL

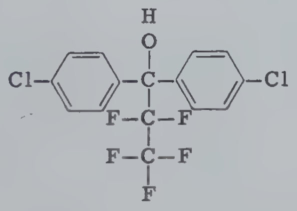
An interesting new departure in the control of Musca is suggested by data indicating that certain substances, appropriately administered to fertilized adult female insects even in sub-lethal dosage, reduce, prevent, or delay oviposition. The compounds show activity when the Musca imagines are exposed to them by tarsal contact prior to the feeding of the exposed females upon milk as a protein source.

COMPOUNDS TESTED

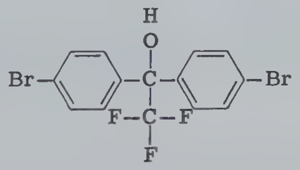
A



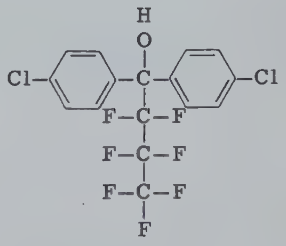
B



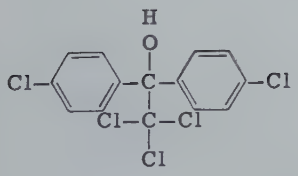
C



D



E



A = Di-(p-chlorophenyl)-trifluoromethyl carbinol
B = Di-(p-chlorophenyl)-pentafluoroethyl carbinol
C = Di-(p-bromophenyl)-trifluoromethyl carbinol
D = Di-(p-chlorophenyl)-heptafluoropropyl carbinol
E = Di-(p-chlorophenyl)-trichloromethyl carbinol

1) Compounds A and B yielded outstanding anti-oviposition activity.
2) Compound C yielded decidedly less anti-oviposition activity than did A and B.
3) Compounds D and E yielded low anti-oviposition activity.
4) Di-(p-chlorophenyl)-dichloromethyl carbinol and di-(p-chlorophenyl)-methyl carbinol (DMC, the acaricide) proved wholly inactive. Replacement of the chlorines in the para-position by methyl- or methoxy- groups in compound A extinguishes the anti-oviposition activity.
5) Compounds A and B possess a slight contact toxicity for Musca domestica and consequently the anti-oviposition activity has been best shown by using a biotype of Musca domestica, Swiss strain K_1, which has a high polyvalent insecticide resistance.
   a) K_1 females are not affected by compounds A and B even under conditions of continuous exposure.
   b) Prior to experimental use, the female flies, 3 days old, are fed on sugar and water only and have been maintained in cages of mixed ♂ and ♀ insects to ensure fertilization.
   c) Experimentally treated flies were found on dissection to harbor abundant spermatozoa in the spermathecae, and to show normally developed ovaries containing eggs, differing in these respects in no way from control female insects.
6) The anti-oviposition effect of the effective compounds is interpreted as being "forced retention" of eggs.

TABULAR SUMMARY OF RESULTS ACHIEVED BY VARIOUS METHODS OF APPLICATION OF COMPOUNDS A AND B TO MUSCA DOMESTICA (BIOTYPE K), 3 DAY OLD FEMALES PREVIOUSLY FED ONLY SUGAR AND WATER:

Mode of Application Of Compounds	Milk Offered	Oviposition Over Whole Lifetime With	
		Compound A	Compound B
Feeding at 0.01% in milk	Daily (treated milk)	Normal	Normal
Exposure to vapours	On 4th day of life	Normal	Normal
Topical at 1 μg/fly in acetone	On 4th day of life	None ①	None ①
Tarsal contact, 30 min, to deposit of $1 g/m^2$	On 4th day of life	None ①	Negligible ①,②
Continuous exposure, contact ③	Daily	Very low	None

① Continuous feeding of milk under conditions of these experiments overswayed the effects on oviposition of compounds A and B.

② Smaller quantities of compounds A and B than those indicated here delayed or reduced drastically the laying of eggs.

③ Filter paper in area = to area of one side of the cage, impregnated with compound A or B at $1.5 g/m^2$, suspended in the center of the holding cage.

OTHER DATA

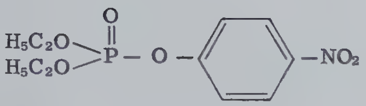
1) Mention is made of data indicating that dieldrin (in sub-lethal doses) increases reproduction potential in Musca domestica and Drosophila melanogaster. A similar effect on Metatetranychus ulmi is claimed for DDT. DDT is reported to reduce oviposition slightly in Drosophila.

Bibliography cited by the source paper:

Bergmann, E. D., et al., Nature (London) 176: 266, 1955.
Kaluszyner, A., et al., Journal of the American Chemical Society 77: 4164, 1955.
Reuter, S., et al., Rivista di parassitologia (Roma) 17: 125, 1956.
Ascher, K. R. S., and Levinson, Z. H., Rivista di parassitologia (Roma) 17: 217,1956.
Afifi, E. D., and Knutson, H., The Journal of Economic Entomology 49: 310, 1956.
Knutson, H., Annals of the Entomological Society of America 48: 35, 1955.
Hueck, H. J., Dissertation, University of Leiden (Netherlands) 1953.
Hueck, H. J., Physiologia comparata et Oecologia 2: 371, 1952.
Tattersfield, F., and Kerridge, J. R., Annals of Applied Biology 43: 630, 1955.

137

PARA-OXON (O,O-Diethyl O-p-nitrophenyl phosphate; Diethyl p-nitrophenyl phosphate; E-600; Mintacol.)



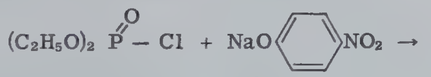
Molecular weight 275.195

GENERAL (Also consult Parathion, Methyl parathion, Organic Phosphates, Systemic Insecticides).
[Refs.: 2769,353,2231,2120,129,713,701,2651,3309,2773,899,3365,1766,672,1801,165,897,373,2867, 703,704]

An insecticide of the general class of organic phosphate or "organophosphorus" insecticides, Para-oxon is closely related to parathion being an ester of orthophosphoric acid while parathion is an ester of thiophosphoric acid. Para-oxon is intensely toxic for insects and phytophagous acarines and has been regarded as too hazardous for mammals to justify use as an insecticide. Para-oxon reveals a much more potent systemic action in the translocation stream of plants than does parathion, a reflection (probably) of a much greater solubility in water. Spray solutions containing para-oxon at 0.001% and 0.005% are respectively the LC_{50} and LC_{100} for certain aphids. Great precautions are dictated in the use of para-oxon because of its intense toxicity. More than twice as toxic as parathion for insects in general. Resistance has been reported for Musca domestica and Tetranychus bimaculatus.

PHYSICAL, CHEMICAL [Refs.: 1339,2773,3309,2231,2120,129,554,3101,85,384]

Technical: A reddish to yellowish oily liquid; pure: A colorless liquid; b.p. (tech.) 148°-151°C at 1 mmHg, (pure) 169°-170° at 1 mmHg; $d^{25°}$ (tech.) 1.269, $d_4^{20°}$ (pure) 1.2736; $n_D^{25°}$(tech.) 1.5060, $n_D^{20°}$ (pure) 1.5105; v.p. (pure) 8.6×10^{-5} mmHg at 27°C; viscosity (tech.) 15.86 centipoises at 25°C; odorless; soluble in water to 2.4 g/l at 25°C, 0.002%, (2400 μg/cc) at 25°C; miscible with most organic solvents and phosphoric acid; moderately soluble in petroleum oils; virtually insoluble in paraffinic hydrocarbons; rapidly hydrolyzes in alkaline media ($K = 0.52\ (OH^-) + 1 \times 10^{-6}\ min^{-1}$), but at pH 5-6 hydrolysis is less than 1% in 62 days; darkens on long exposure to sunlight; prepared from diethyl chlorophosphate and sodium paranitrophenate:



The compound shown above.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Decidedly more toxic than parathion for mammals; has a high toxic hazard. 165,897

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Frog	sc	MLD	30	Given in water + cellosolve.	1475
Mouse	sc	MLD	2	Given in oil solution.	1475
Mouse	sc	MLD	0.6-0.8	Given in water + cellosolve.	1475
Rat	or	MLD	3	Given in water + detergent.	1475
Rat	or	LD_{50}	3.5		857
Rabbit	ct	LD_{50}	5	Single acute exposure.	2231

   b) In the animal body parathion is converted into a substance with greater anti-choline esterase activity than the parent; this substance has been identified as para-oxon. ID_{50} concentration of purified para-oxon for ChE = 2.01×10^{-8}M. 1090, 31

2) Chronic toxicity; higher animals:
   a) No data ad hoc are available to this compilation; consult parathion.

3) Phytotoxicity:
   a) In a comparison of 4 systemic insecticides (para-oxon, BFPO, OMPA, sodium fluoroacetate) para-oxon was reported the most phytotoxic and was said to have the narrowest margin of safety between the insecticidal and phytocidal concentrations; the order of increasing toxicity when applied to roots of plants in sand or soil culture: 701

      Sodium fluoroacetate < BFPO < OMPA = (ca.) para-oxon.

      (1) Para-oxon (like OMPA) is reported to bring about biochemical changes in plants similar to those induced by 2,4-D, namely an increase in the carbohydrate content of beans and peas the effect being more pronounced in sunlight than in darkness. 672

4) Systemic action in plants:

a) Para-oxon after uptake by the plant remains present (as such) in the performance of toxic action until decomposed by the plant into non-insecticidal metabolites and is classed as an endolytic, systemic toxicant. 2651

(1) By some the systemic action is reported undetectable. 701

(2) Others report an appreciable systemic action. 672

b) 7% of the para-oxon applied to treated parts of a plant (bean, maize) is stated to be present in unsprayed leaves 12 days after application (in contrast with 40% for OMPA or its active derivative). 672

(1) The directional movement in the treated plant (foliage application) is either up or down in the translocation stream.

(2) Translocation of para-oxon in Vicia faba or Zea mays after foliage application, is less than for OMPA, more than for parathion.

(3) Translocation is minimal in the blooming Vicia faba as compared with actively growing plants in the 6 to 10 leaf stage.

c) Time required for 100% kills of Tetranychus bimaculatus on leaves of Vicia and Zea with petiole or cut end in solutions of para-oxon and other compounds; temperature: Vicia 60-90°F, Zea: 62-86°F. 672

Compound	Concentration (%)	Hours For 100% Kill On	
		Zea mays	Vicia faba
Para-oxon	0.005	120 ± 6	48 ± 5
"	.02	72 ± 5	18 ± 2
"	.05	48 ± 5	12 ± 3
Parathion	.005	< 100% in 96 hrs.	60 ± 4
"	.02	"	40 ± 2
"	.05	120 ± 8	30 ± 3
OMPA (Schradan)	.005	48 ± 2	48 ± 5
	.02	45 ± 2	30 ± 3
	.05	40 ± 3	24 ± 2

d) Mortality (in 1 week) of Tetranychus bimaculatus on leaves of untreated Vicia faba plants, placed under bell jars with treated plants at 60°-80°F, 300 mites per test, 3 replicates. Fumigant action via systemic route. Plants foliage treated: 672

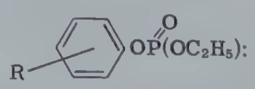
Compound	(Concentration (%)	Corrected Mortality (%) 1 Week
Para-oxon	0.05	29 ± 5
"	.02	12 ± 4
Parathion	.05	68 ± 8
"	.02	29 ± 5
OMPA	.05	3.5 ± 2
	.02	0

(1) Plainly the systemic action of para-oxon is distinctly less important than its contact action vs. insects.

5) Toxicity for insects; acarines:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti (larva)	Medium	LC_{50}	0.007 ppm		672
Aëdes aegypti (larva)	Medium	LD_{90}	0.016 ppm		672
Anopheles quadrimaculatus (4th instar)	Medium	MLC_{100} 24 hr.	0.025 ppm	82% kill at 0.01, 50% at 0.005 ppm.	1766
Apis mellifera (adult)	Topical	LD_{50}	0.6 μg/g	LD_{50} for diethyl o-nitrophenyl phosphate = 1 μg/g.	2244
Ceratitis capitata (adult)	Topical	LD_{50}	0.23 μg/g		2659
Dacus cucurbitae (adult)	Topical	LD_{50}	0.53 μg/g		2659
Dacus dorsalis (adult)	Topical	LD_{50}	0.37 μg/g		2659
Musca domestica (adult)	Topical	LD_{50}	0.5 μg/g	LD_{50} for diethyl o-nitrophenyl phosphate = 7 μg/g.	2244
M. domestica (Laboratory I strain)	Topical	LD_{50} 24 hr.	2.6 μg/g	In acetone; origin of strain: NAIDM.	373
M. domestica (Laboratory II strain)	Topical	LD_{50} 24 hr.	1.9 μg/g	" ; " : Univ. of Indiana.	373
M. domestica (DDT-I strain)	Topical	LD_{50} 24 hr.	3.8 μg/g	" ; 21 generations selection vs. DDT.	373
M. domestica (Methoxy-I strain)	Topical	LD_{50} 24 hr.	2.3 μg/g	" ; " vs. Methoxychlor.	373
M. domestica (Multi-I strain)	Topical	LD_{50} 24 hr.	6.2 μg/g	" ; resistant to several chlorinated hydrocarbons.	373
M. domestica (Para-oxon I strain)	Topical	LD_{50} 24 hr.	10.06 μg/g	In acetone; 8 generations exposure to para-oxon.	373
M. domestica (laboratory strain)	Topical	LD_{50} 24 hr.	0.045 μg/fly	At 80°F.	371
M. domestica (Para-oxon strain)	Topical	LD_{50} 24 hr	> .51 μg/fly	At 80°F; a strain selected against para-oxon.	371
Periplaneta americana (adult)	Topical	LD_{50}	0.75 μg/g	Effectiveness varies with solvents:	2244
Periplaneta americana (")	inj	LD_{50}	0.65 μg/g	Propyleneglycol > ethanol > dioxane > benzene.	2244

b) Comparative toxicity of certain diethyl aryl phosphates; 

2244

R	Topical LD_{50} (μg/g) For		ID_{50}, Apis Brain Choline esterase
	Musca domestica	Apis mellifera	
H-	> 500	> 1000	3 x 10^{-4} M
p-CH_3-	> 500	200	6.2 x 10^{-6} M
p-$(CH_3)_3C$-	> 500	> 100	1.1 x 10^{-4} M
o-Cl-	250	> 100	5.7 x 10^{-5} M

R	Topical LD_{50} (μg/g) For		ID_{50}, Apis Brain Choline esterase
	Musca domestica	Apis mellifera	
p-Cl-	150	> 100	4.2×10^{-4} M
o-NO_2-("ortho-Para-oxon")	7	1	3.3×10^{-7} M
p-NO_2-(Para-oxon)	0.5	0.6	1.9×10^{-8} M
2,4-diNO_2-	155	75	2.9×10^{-7} M
2-NO_2-, 4-Cl-	23	10	3.4×10^{-7} M
Parathion	0.9	1.47;3.5	

c) Toxicity of Para-oxon and other insecticides to the overwintering eggs of Aphis pomi and Operophtera brumata; 10 second immersions at various concentrations with 100 - >300 eggs per trial: 899

Compound	% Mortality At Concentrations Of			
	0.2%	0.05%	0.2%	0.05%
	Aphis pomi		Operophtera brumata	
p-Nitrophenyl diethyl phosphate (Para-oxon)	99.6	100	7.8	4.4
p-Nitrophenyl diethyl thionophosphate (Parathion)	100	78.6	95.4	90.8
Triethyl phosphate	1.4	0	3.1	7.1
Triphenyl phosphate	14.1	0	8.0	6.4
Tri-o-tolyl phosphate	0	7.1	5.8	7.9
Triphenyl phosphine	13.9	5.1	3.4	3.6
HETP	7.4	1.1	6.2	3.7
Diethyl acetyl phosphate	5.7	8.4	8.7	1.3
Diphenyl ethyl thionophosphate	0	8.1	8.5	4.8
p-Nitrophenyl dichlorothionphosphate	40.4	10.3	—	10.2
Diphenyl chlorothionphosphate	25.9	4.9	4.0	3.0
Tri-(p-nitrophenyl) thionophosphate	5.3	0.6	1.9	4.3

d) Comparative toxicity of Para-oxon and other compounds vs. Anopheles quadrimaculatus 4th instar larvae; insecticides as acetone-water suspensions: 1766

Compound	% Mortality In 48 hr. At							
	0.1 ppm	.05 ppm	.025 ppm	.01 ppm	.005 ppm	.0025 ppm	.001 ppm	.0005 ppm
Para-oxon	100	———	———	82	50	—	—	—
Sulfotepp®	100	———	———	———	———	———	74	34
Parathion	100	———	———	———	———	96	56	34
EPN®	100	———	———	———	———	96	32	—
Methyl parathion	100	———	———	———	———	67	—	—
O,O-dimethyl-(2-chloro-4-nitrophenyl thiophosphate	100	———	———	96	86	62	62	44
Malathion	100	———	96	80	80	60	40	24
Ortho-EPN	100	———	———	———	70	80	4	—
Diazinon	100	———	———	———	36	20	—	—
O,O-Dimethyl O-(3-chloro-4-methy-umbelliferone) thiophosphate	100	———	———	64	46	24	—	—
Chlorthion®	100	———	88	76	44	—	—	—
Potasan®	100	98	56	30	5	—	—	—
O,O-Diethyl O-piperonyl thiophosphate	100	94	58	26	—	—	—	—
NPD	94	—	62	30	—	—	—	—
DDT	—	—	—	100	94	49	24	—

6) Resistance to para-oxon in insects:

a) By repeated exposure of the larvae and adults of a wild biotype of Musca domestica, a biotype with greatly enhanced resistance has been selected (see the tabulation of quantitative toxicity). 373

b) Vs. certain greenhouse "populations" of Tetranychus bimaculatus, concentrations of para-oxon (as an aerosol in methyl chloride) which normally gave 100% kills yielded only 6% kills. 2867

7) Pharmacological, pharmacodynamic, physiological etc; insects:

a) The action of para-oxon (as of other organic phosphate toxicants) in the poisoning of arthropods is presumed to be linked ultimately to the capacity to inhibit or block acetylcholine- and/or other choline-esterase(s). The in vitro inhibition of insect brain choline esterase(s) by para-oxon has been repeatedly demonstrated. 2244 2231 353

b) Para-oxon readily enters the cuticle of insects (cf. the high contact [topical] toxicity); the solvent has much to do with rate of penetration. Tested on the cervical membrane of Periplaneta americana, para-oxon penetrated rapidly (50-80% was in the insect within 5 minutes). 2244

(1) Order of solvent effectiveness: Propylene glycol >ethanol >dioxane >benzene; at minimum, penetration was 60% in 1 hour of contact.

c) Para-oxon is approximately equally toxic by injection or topical application in Periplaneta and Apis. 2244

d) Para-oxon undergoes rapid transport in the insect body (Periplaneta) and compared with others the distribution by the insect hemolymph after topical application varies directly as the water-solubility. 989 2657

e) Para-oxon has been identified chromatographically among the products of the incubation of parathion with Periplaneta gut and is deemed responsible for in vivo anticholine esterase activity of Parathion. 2248 2243

f) Replacement of the diethyl- of para-oxon by dimethyl- to give methyl-para-oxon enhances the toxicity for Apis mellifera two-fold. 2231

8) Miscellaneous:

a) Use of para-oxon (a non-selective insecticide) has been followed by rapid resurgence of aphid "populations" within 14 days after application, due to decimation of natural predators. 2650

b) Compared with sodium fluoroacetate, bis-dimethylaminophosphonous anhydride and BFPO, para-oxon proved to be the only one outstandingly toxic to the eggs and larvae of Pieris brassicae. 703

(1) Applied in water to roots of cabbage, para-oxon killed the eggs in egg batches on the leaves, death occurring when the young larvae were biting through the shell.

(2) 20 cc of a solution containing 0.001 cc of para-oxon on moist soil (400 g) with a 6-8 leaf cabbage plant gave 95% kills of eggs (by failure to hatch) and 100% kills of larvae from eggs which succeeded in hatching. A solution with 0.002 cc para-oxon killed 100% of tested 3rd instar Pieris larvae.

c) Systemic action of para-oxon vs. Phaedon cochleariae compared with that of schradan, dimefox and sodium fluoroacetate. 704

(1) Compared by direct contact toxicity the order of effectiveness was: Para-oxon > sodium fluoroacetate = dimefox > schradan (with adults being more resistant than larvae).

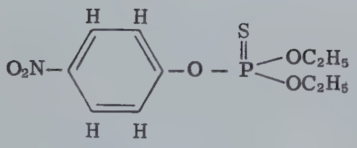
(2) Comparison of toxicity by systemic action: Order of toxicity was: Para-oxon > dimefox > sodium fluoroacetate = schradan (with para-oxon and dimefox yielding 100% kills at practicable concentrations).

(3) Approximate concentrations to yield 100% kills of Aphis, Pieris (3rd instar) and Phaedon (adults): by dipping and by systemic action:

Insecticide	Dipping (% Concentration)			Systemic, From The Soil; (cc/3½ Inch Pot Containing 400 g Compost Soil).		
	Aphis	Pieris	Phaedon	Aphis	Pieris	Phaedon
Para-oxon	.0005	.01	.01	>.04 (grams)	.002 (grams)	.002 (grams)
Sodium fluoroacetate	.001	>.1	>.1	.001	.02	>.1
Dimefox®	.05	>.1	>.5	.002	>.02	.01
Schradan	.05	>.2	>1.0	.02	>.04	>.1

138

PARATHION (O,O-Diethyl O-p-nitrophenyl thiophosphonate; O,O-Diethyl O-p-nitrophenyl phosphorothioate; O,O-Diethyl O-p-nitrophenyl thiophosphate; Diethyl p-nitrophenyl monothiophosphate; E-605; Compound 3422; Thiophos; Niran; Alkron; Genithion; Penphos; Phos-Kil; Vapophos; SNP; DNTP; DPP, etc.)



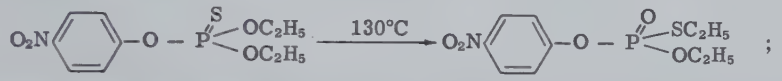
Molecular weight 291.27

GENERAL (Also consult Methyl parathion, Para-oxon, Chlorthion, Organic Phosphate Insecticides, in this work) [Refs.: 1176,1949,1718,852,714,89,1458,353,2231,520,1801,851,206,1221,1135,2120,129,2126,1164, 904,1719,1306,2862,1404,775,2247,1358,2033,1286,2305,1766,899,3365,3267,3376,307,675,2275, 3245,1102,2864,1915,2128,30,1753,1213,2345,2699,1597,2119,1298,774,1996,1244,2650]

A member of the general class commonly called the organic phosphates or "organophosphorus" insecticides, parathion (developed by G. Schrader in 1944) was first generally described in 1946. Parathion has been one of the first of its class of insecticides to achieve wide practical use as a substance available in commerce. Parathion is intensely toxic by contact, by mouth, and to some extent by fumigant action to most insects and plant-eating acarines. Parathion is of high mammalian toxicity and when employed without precaution and due care for personal protection is exceedingly hazardous. Employed primarily in agriculture (in field and hothouse use), the hazard of parathion is particularly directed toward spraying and insecticide handling personnel and those in industrial plants engaged in its synthesis formulation or "packaging." Human fatalities and severe poisonings have followed ingestion and skin exposure alone and inhalation accompanied by various degrees of skin exposure. Employed as an instrument of suicide or murder, it has been the cause of deaths to all intents and purposes instantaneous. With all regard to its toxic properties for higher animals, parathion, like other intensely toxic agents such as nicotine, cyanides, arsenates etc., has been used safely and with notable success as one of the most interesting of contemporary insecticides and acaricides. Around parathion has grown a large body of published data.

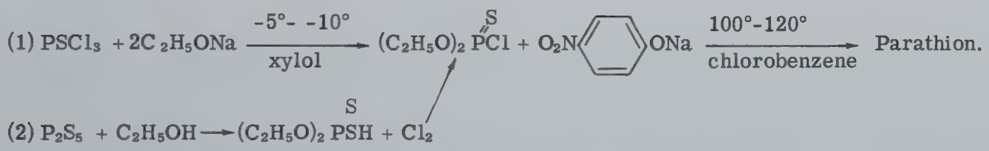
PHYSICAL, CHEMICAL [Refs.: 2231,2120,129,353,340,498,3309,2771,2773,3101,554,1784,1030,1031,2464, 2248,2247,3365,2769,205,143,2332,1694,3157,3163]

A colorless, almost odorless liquid (pure); a yellow to dark brown liquid with a pungent, garlic-like smell (technical, commercial); m.p. 6.1°C; b.p. 157°-162°C at 0.6 mmHg, 375°C at 760 mmHg; $d_{4°}^{25°}$ 1.265; $n_D^{20°}$ 1.53668; v.p. 3.78×10^{-5} mmHg at 20°C, 0.0006 mmHg at 25°C; virtually insoluble in water (20 ppm, 0.00002%, 24 μg/l at 25°C) miscible in all proportions with most acids, alcohols (to 6 carbon), esters, ethers, ketones, aromatic hydrocarbons (benzene, toluene, etc.) chloroform, carbon tetrachloride, animal and vegetable oils; practically insoluble in petroleum oils (petroleum ether, kerosene), paraffinic oils and the usual spray oils; soluble to a limited degree in phosphoric acid; rapid hydrolysis in alkaline media ($K = 0.047\ (OH^-) + 4 \times 10^{-6}\ min.^{-1}$ at 25°C) but at pH 5-6 only 1% is hydrolyzed in 62 days at 25°C; in water, hydrolysis is 50% complete in ca. 120 days; products of hydrolysis in aqueous media: p-Nitrophenol, diethyl orthophosphoric acid; darkens on exposure to sunlight; incompatible with alkaline agents, for instance lime, lime-sulfure, Bordeaux mixture, calcium arsenate; use with cryolite, Paris green, dinitro-compounds is questionable; virtually non-corrosive; decidedly sensitive to isomerization under heat:



the isomer shown may be present to considerable amount in technical or commercial samples of para-oxon (q.v.); S-ethyl O,O-bis(p-nitrophenyl) thiophosphate, may also be present; the nitro-group is easily reducible to amino- by hydrogen.

Preparation:



Formulations: Wettable powders; dispersible powders; aerosols (for glasshouse use only); dusts; emulsifiable concentrates; pyrotechnic preparations ("smokes").

Residues on Crops: Deposits, originally at 20 ppm, fell to 1 ppm in 10 days, 0.1 ppm in 30 days following 3255
application. Applications at normal insecticidal levels fell to 1 ppm in 15-20 days following final treatment. 475
Soil accumulation is of little importance and falls below 1 ppm in 4 to 6 weeks. Residue on kale at 150 lbs/acre = 1186
3 ppm and at this level proved non-toxic to Guinea pigs. After application to citrus, residues are found in the 129
rind oils not in the pulp. 2-5 ppm are not considered to constitute a residue hazard. Not to be applied within 1950
less than 21 days of harvest to Lima beans, beets, dry beans, melons, carrots, squash; within 15 days to peppers, 58
peas; within 21 days to snap beans, cabbage, broccoli, Brussels sprouts, kale, mustard, turnip, celery, cucumber,
onion, potato, tomato, okra, egg plant, spinach, artichoke, or within 12 days of picking (or harvest for forage) of
corn.

a) Residual half-life in citrus peel = 60-80 days 1302

TOXICOLOGICAL [Refs.: 65,771,1114,1279,1473,1686,1754,1936,2270,2383,2387,2442,94,3065,3071,3148,3306, 3311,3312,189,682,756,793,826,855,856,948,949,950,1460,1570,2731,3167,3168,]

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Frog	sc	MLD	200	In cellosolve + water.	1475
Mouse	sc	MLD	20	In vegetable oil.	1475
Mouse	sc	MLD	10-12.5	In cellosolve + water.	1475
Mouse	sc	LD_{50}	15-25		3148
Mouse	or	LD_{50}	25 ± 1.8		1057
Mouse	ip	LD_{50}	5.5		861
Rat	or	LD_{50}	4.42	In corn oil.	746
Rat	or	LD_{50}	4.03	"	746
Rat (and Mouse)	or	LD_{50}	12-24	As the water wettable powder.	57
Rat	or	MLD	6.4	In water + detergent.	3148
Rat ♀	or	LD_{50}	3.5		1462
Rat ♂	or	LD_{50}	12.5		1462
Rat ♀	or	LD_{50}	3.0 ± .25		1057

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat ♂	or	LD$_{50}$	30.0 ± 3.6		1057
Rat ♀	or	LD$_{50}$	6		129
Rat ♂	or	LD$_{50}$	15		129
Rat ♀	ip	LD$_{50}$	4		857
Rat ♂	ip	LD$_{50}$	7		857
Rat ♂	iv	LD	3	As an ethanol solution.	30
Guinea Pig	or	LD$_{50}$	32 ± 2		1057
Rabbit	ct	LD$_{100}$	140	At 15°-25°C	3148
Rabbit	ct	LD$_{50}$	870	As the pure substance.	1653
Rabbit	ct	LD$_{50}$	420	In corn oil solution.	1653
Rabbit	ct	LD$_{50}$	40-50		2231
Cat	ip	LD$_{50}$	3-5		857
Dog	ip	LD$_{50}$	12-20		857
Horse (ca. 700 k)	or	LD	3500 mg/animal		776
Laboratory Animals	ct	LD$_{50}$	30-60		129
Man (ca. 70 k)	or	LD	20 mg/man		776
Bluegill	Medium	Threshold	0.2 ppm		2026
Bluegill	Medium	LC	0.063 ppm	Some individuals.	3020
Goldfish	Medium	LC$_{50}$	1.5 ppm	5 day exposure (DDT = .125 ppm)	1176
Goldfish	Medium	LC$_{100}$	2.0 ppm	" (DDT = .25 ppm)	1176

a) Comparative toxicity parathion and isomers: 2126

Substance	Average Lethal Dose (mg/k) sc, Rat	LD$_{50}$ (mg/k) sc Mouse	
		(Schrader)	(Hecht and Wirth)
Parathion	50	18	10-12.5
S-ethyl-isomer	5	50	20
S-phenyl-isomer	1	50-100	1.25

(1) Tolerated dose (U.S.) 2 ppm; no cumulative action at less than 5 ppm. 1057

(2) Average acute LD$_{50}$ (all animals tested) 3.5 mg/k; minimum in diet for death or severe injury as 1949
chronic toxicant 25 ppm; danger level (cutaneous) 50 mg/k. Single oral lethal dose (estimate) for man 852
ca. 100 mg.

Hazard: 1648,2943

(1) May be absorbed by mouth, dermal contact, inhalation, or combinations of these. The eye is a 2958,3077
particularly sensitive avenue (LD absorbed [with death in 3 minutes] rabbit). Little warning of 124,89,353
skin exposure; parathion is virtually non-irritant. 2231,129

(2) Death has followed splashing of skin or clothing with the tech. liquid in amounts insufficient to drench, or lead the victim to bathe or change clothes. 89

(3) In several human fatalities intake was 900 mg; the acute oral dose for man (based on animal experiences) 12-20 mg (.2-.33 grains); acute LD, dermal = ca. 3 times the oral dose. 89

(4) Inhalation hazard: After application, low vapor pressure (3.78 x 10^{-5} mmHg) renders vapor hazard 1458
unlikely. Mild to severe intoxications have occurred among mixing plant workers, applicators and 3010
orchard workers with sharp decline in choline esterase levels and with near fatalities in cases of 361
massive exposure or carelessness rather than as result of long sub-acute exposures. Continuous 1837
exposure to 2 to 8 mg per 10 m^3 air (a level found in manufacturing and mixing plants) is potentially 474
hazardous. Mild intoxications were induced in animals with "saturated vapors." Vapors in air 86
passed at high temperature through tech. parathion were not toxic to rats and proved ineffective in reducing choline esterase levels. Vapors from treated crops, for instance from orange fruits, are not toxic to flies. Inhaled particulate parathion (aerosols, impregnated dusts, parathion-bearing materials) is acutely and severely toxic and such inhalation is a distinct and serious hazard. Inhaled 15% dusts are uniformly fatal to animals.

(5) Chronic exposure hazard: Parathion is not cumulative in the strict sense. No storage in the body, 89,1753
little, if any, tissue damage. However, parathion exposure lowers choline esterase levels; small, 1462
repeated dosages are more or less additive, and the organism remains relatively susceptible (de- 353
pending on degree of exposure) to low dosages and brief exposures until choline esterase is regenerated.

(6) Human fatalities, intoxications: Consult [2550,1917,88,579,580]. In one case 120 mg were swallowed; paralysis came so swiftly that the victim proved unable to take advantage of antidotes near at hand. Citrus workers have been routed from dusty treated orchards; peach thinners, working 2 days after spraying of trees, have required hospitalization.

2) Chronic and sub-acute toxicity; higher animals:

a) Rats:

(1) ♀♀ receiving in diet 50 ppm: Normal gestations and rearing of young; ♂♂ at 100 ppm in diet: Survived 57
indefinite exposure; ♂♂ exposed 2 years to 100 ppm in diet: No effect on growth, food consumption, 1462
weight gain, no increase beyond normal mortalities, no histopathological changes; lifetime exposures 579
to 25 ppm in diet: Normal survival without effect; nervous symptoms, choline esterase-level decline, 580
begin at dosages greater than 25 ppm.

b) Dogs:
(1) No overt symptoms at 1-3 mg/k/day. 57

c) Cows:
(1) In mid-lactation, receiving alfalfa with 14 ppm residue content for over 61 days (av. parathion intake 166.9 mg/cow/day, 0.33 mg/k/day): No deleterious effects in milk production, weight maintenance, general health. 2437

d) Farm animals:
(1) Negative results reported from feeding of parathion treated forage crops. 1850

3) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:

a) Acts in vivo as a cholinergic toxicant inhibitory of choline esterase activity permitting 89,1221,851,24,857
extensive accumulation of acetylcholine with consequent cholinergic signs. 1278,2244,31,794,2247
(1) Some effects are not related directly (nor perhaps alone) to choline esterase inhibition.

b) Not, in vitro, an active choline esterase inhibitor; such activity in vitro now known to be due to impurities. Pure parathion is inactive in vitro toward choline esterase.

c) Converted, in vivo, chiefly (?) by the liver to a metabolite intensely active against choline 30,1090,2248,2243
esterase(s), and identical to para-oxon (q.v.) 795,1089,1846,2335
(1) The in vivo toxicity of parathion is reduced by hepatectomy.
(2) ♂♂ rats are decidedly less sensitive toward parathion than are ♀♀. 857
(3) Isomerization to O,S-diethyl O-p-nitrophenyl thiophosphate does not alter cutaneous toxicity for 2231
the mouse, but reduces sharply oral toxicity for the rat.

d) ID_{50} (concentration for 50% enzyme inhibition) values in vivo: vs. vertebrate choline esterase(s): 1278,863

Human plasma choline esterase	1.5×10^{-6} M
Human erythrocyte choline esterase	1.2×10^{-5} M
Rat brain choline esterase	1.2×10^{-6} M

e) Symptomatology:
(1) Symptoms appear when exposure to parathion, by any portal of entry, reduces choline esterase levels 89
below a critical point, in general to ca. 30% of the normal pre-exposure level. 714,237
(2) Unless the exposure is fatal, recovery appears complete in time after regeneration of choline esterase 89
to the critical quota. Regeneration is de rigueur because the choline esterase inhibition by parathion is irreversible.
(3) CNS, parasympathetic and sympathetic-based symptoms may all be present at one or another phase of 237
intoxication. 1458
(4) Nicotinic signs: (Autonomic, sympathetic): Due to stimulation followed by paralysis of striated muscle. 237
(5) Muscarinic effects: Attend excessive stimulation of autonomic effector cells. In man these may include: 714
Anorexia, nausea, vomiting, abdominal cramp-like pain, profuse sweat, salivation followed by: Pallor, 89,475
miosis, diarrhoea, involuntary urination, defecation (failure of sphincter control) lung oedema, 1333
cyanosis. Animal symptoms (acute poisoning): Lachrymation, profuse salivation, intestinal hyper- 1353
motility + diarrhoea, generalized fibrillary tremors, death in respiratory failure within the day.
(6) CNS signs: Usually early in human poisonings: Giddiness, restlessness, severe headache; in serious 3045
cases: Ataxia, tremors, drowsiness giving way to coma; convulsions in coma. 89
(7) Vs. CNS and muscarinic symptoms atropine is the specific antidote; vs. the nicotinic symptoms 237
(announced by twitchings of eyelids and tongue spreading to face and neck then becoming finally 89
generalized over the skeletal musculature and followed by weakness and paralysis of striated muscle) 714
no antidote is known: 852
(8) Course of typical parathion poisoning in man: (Death from massive dosages either in suicide, homicide, 89
gross carelessness, accident, is essentially instantaneous.) Onset of symptoms slower than with TEPP, 237
HETP (q.v.); anorexia, nausea (enhanced by food, smoking) appear in $\frac{1}{2}$ to 2 hrs. followed by: Vomiting, cramps, salivation, sweating; giddiness, restlessness may precede (as initial signs of poisoning) or follow anorexia and nausea; in mild cases (unless the eye is involved directly as portal of entry) pupillary constriction (too often relied on as a prime symptom of organic phosphate insecticide exposure) may be absent; twitching of eyelids and tongue follows nausea and vomiting; general muscular twitching and voluntary muscle weakness followed by death in respiratory paralysis may develop in spite of adequate atropinization; ataxia, tremor, drowsiness, impaired concentration and reasoning, confusion, disorientation and slurred speech are late signs; in mild cases sometimes causes insomnia and unusual dreaming; the initial giddiness and apprehension are followed usually by severe headache; coma is usual in from 1 to 9 hours following onset, with death from 1 to 21 hours after the last exposure and, as an average, 9 hours after the first symptoms.
(9) Treatment: Morphine, theophylline, aminophylline strictly contra-indicated. Adequate atropinization, 89
careful and continuous observation of the victim during the 24-48 hours of acute emergency. Even 713
after late signs, viz., loss of reflexes, failure of sphincters, coma and convulsions energetic treatment 714
may yield survival. Relapse is possible at every stage, requiring constant watch over victim. Follow- 237
ing any exposure productive of symptoms, further exposure must be guarded against, since hyper- 853
susceptibility endures until choline esterase is regenerated. Atropine or physostigmine pretreatment 1333
raises the LD by 6-8 times.

f) Metabolic:
(1) p-Nitrophenol is the principal metabolite of parathion; p-nitro- and p-aminophenol appeared in urine 2308,1112
after sub-toxic doses (plasma ChE inhibited but no overt toxic signs). 1989,3215
(2) Lactating cows fed parathion (commercial wettable powder) in capsules 32 mg/k/day showed: 2437
No free parathion, free p-nitrophenol or p-aminophenol in jugular blood, urine, milk. Indications

are that: Parathion hydrolyzed in vivo → p-nitrophenol → reduced to p-aminophenol $\xrightarrow[\text{with}]{\text{conjugated}}$ glucuronic acid → excreted as p-aminophenyl glucuronide. Fate of thiophosphoric moiety undetermined.

(3) Cows, fed at levels greatly above normal on forage residues (e.g. 166.9 mg/cow/day over 61 days), showed no free parathion or p-nitrophenol in jugular blood, milk or urine. 2437, 681

(4) S^{35} labelled parathion fed to rabbits: S^{35} appeared promptly in urine after cutaneous or intravenous application; no storage; S^{35} appeared not as parathion but as a metabolite. 1694, 1693

(5) In vivo parathion is converted to an oxygen analogue; S is freed, being replaced by O; S is excreted via urine; aromatic -NO$_2$ is hydrolyzed and excreted as p-aminophenol and p-nitrophenol; fate of phosphate unknown, although the phosphate nucleus alters the enzyme kinetics. 794, 2243

g) Histopathology: Tissue damage typical of enterocolitis and gall bladder necrosis have been reported. No significant gross or microscopic pathology is to be expected save such as may be associated with pulmonary and cerebral oedema or changes attendant on convulsions. 1949, 89

4) Hazard to vertebrate wild-life:

a) 10 times as toxic as DDT, vs. rainbow trout, salmon, grayling. 3114

b) Applied to wheat fields at 0.25 lb per acre produced no mortality among wild birds and other animals frequenting such fields. 353

5) Phytotoxicity:

a) Most garden and glasshouse plants withstand large amounts; cucumber and tomato are sensitive. 57

b) 500 species of plants, tested with aqueous sprays 0.02-0.03% parathion were unharmed; foliage of ferns injured; Poinsetta bracts and Saintpaulia flowers damaged; leaf-drop of roses; 3% dusts produced transient symptoms on squash. 2550

c) Orchard foliage is, in general, safe except at high concentrations under cool, humid conditions. 2524,84

(1) McIntosh and Cortlandt apples are sensitive to >0.01%; foliage and fruit necrosis are reported. 57,1198,1799

(2) 0.05% has damaged plum tree foliage. 1606

d) Application in oil solution increases hazard for certain shrubs at 0.02%. 2794

e) Applied to soil at .25, .5, 1.0, 2.0 g per 500 g soil (dry wgt.): No effect on germination save at 1.0, 2.0 g; slight growth retard first 2 weeks (pronounced at 2.0 g) thereafter normal in Nasturtium.

f) 200 ppm in the soil rendered leaves of corn toxic to Pyrausta nubilalis without phytotoxicity. 2564

g) 600 ppm in soil (1 to 10 days before seeding) protected Nasturtium from aphids without phytotoxicity.

h) On 3 week old tobacco at an excessive amount (22.7 lbs/acre) caused serious stunting and high mortality of plants; 1 month later no residual insecticidal effect noted. As a pre-sowing application at 2% dust concentration, 1.8 lbs per acre: No harm to tobacco plants. 123

i) Thus phytotoxic hazard is (in general) low, save to some ornamentals, apples, and under certain weather conditions, to pears; damage to McIntosh apples is avoided by addition of activated charcoal; 50 to 100 lbs per acre in soil is harmless to vegetables except muskmelons and snap beans. 2120, 129

j) A plant stimulating effect (nutritional?) has been noted in some plants, such as potatoes and corn, even at non-insecticidal levels. 3355

6) Toxicity for insects:

Parathion is perhaps the most generally potent insecticide presently in commerce. A powerful acaricide. Notably effective against aphids, mites, lepidoptera, coleoptera, leaf hoppers, thrips, curculio, codling moth, scale insects, leaf miners, mealy bugs and symphilids. LC$_{100}$ for certain aphids as a contact spray solution = 0.001%; at 0.05-0.1 lb per acre has controlled DDT-R Aëdes taeniorhynchus. Less than $\frac{1}{2}$ as insecticidal as para-oxon, q.v., but more stable and less toxic for animals. 2244, 899, 165, 2076, 897

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti (larva)	Medium	LC$_{100}$	0.0006 ppm		1427
Aëdes aegypti (3rd instar larva, pupae)	Medium	100% kill 48 hrs.	.005 ppm	DDT = 0.05 ppm.	1176
Aëdes aegypti (")	Surface Applic.	100% "	.0006 lbs/acre	Surface application in oil.	1176
Aëdes aegypti (3rd instar larva)	Surface Applic.	100% "	.005 lb/acre	" as dusts.	1176
Aëdes aegypti (pupae)	Medium	100% kill 24 hrs.	1.0 ppm	DDT LC$_{100}$ 24 hrs. = 230 ppm. DDT LC$_{50}$ 24 hrs. = 25 ppm.	1176
Aëdes aegypti (")	Surface Applic.	100% "	0.2 lb/acre	In oil as surface application.	1176
Aëdes aegypti (")	Surface Applic.	50% "	0.1 lb/acre	Surface application as dusts.	1176
Anasa tristis (adult)	Topical	LD$_{100}$ 72 hr.	32μg/g	In acetone solution.	3376
Anopheles quadrimaculatus (larva) 4th instar	Medium	MLC$_{100}$	0.005 ppm	96% mortality at 0.0025 ppm.	1766
Aphis rumicis	or	LD$_{50}$	0.0005μg/insect, 0.8μg/g		1119
Apis mellifera (adult)	or	LD$_{50}$	0.1μg/bee, 1.0μg/g		1119
Apis mellifera (")	or	LD$_{50}$	0.07μg/bee		910
Apis mellifera (")	or	LD$_{50}$	0.08μg/g		206
Apis mellifera (")	Topical	LD$_{50}$	1.47μg/g		206
Apis mellifera (")	inj	LD$_{50}$	0.94μg/g		206
Apis mellifera (")	or	LD$_{95}$	0.2μg/g		206
Apis mellifera (")	Topical	LD$_{95}$	1.67μg/g		206
Apis mellifera (")	inj	LD$_{95}$	3.47μg/g		206
Apis mellifera (")	or	LD$_{20}$ 24 hr.	0.018μg/bee	In 50% sugar solution.	1718
Apis mellifera (")	or	LD$_{50}$ 24 hr.	0.04μg/bee	"	1718
Apis mellifera (")	or	LD$_{90}$ 24 hr.	0.144μg/bee	"	1718
Apis mellifera (")	Contact Spray	L Deposit$_{20}$	0.257μg/cm^2		1718
Apis mellifera (")	Contact Spray	L Deposit$_{50}$	0.354μg/cm^2		1718
Apis mellifera (")	Contact Spray	L Deposit$_{90}$	0.574μg/cm^2		1718
Apis mellifera (")	Residual	L Deposit$_{90}$	0.54μg/cm^2	1 hour contact with dry film.	1718
Apis mellifera (")	Residual	L Deposit$_{10}$	0.18μg/cm^2	"	1718

Insect	Route	Dose	Dosage	Remarks	
Apis mellifera (adult)	Vapor from Residues	L Deposit$_{100}$ 24 hr.	5.0μg/cm^2	Exposure 1 hour.	1718
Apis mellifera (")	"	L Deposit$_0$ 24 hr.	2.8μg/cm^2	" .	1718
Chaitophorus populi	Contact Spray	LC$_{50}$	0.008 g/l	Dusting tower application.	775
Cirphis unipuncta (larva)	Topical	LD$_{50}$	3.7μg/g	Ratio LD$_{50}$: LD$_{99}$ = 3.4.	3268
Cirphis unipuncta (larva)	or	LD$_{50}$	2.5μg/g	On treated leaves; ratio LD$_{50}$: LD$_{99}$ = 8.5 Field concentration = 360 ppm.	3268
Conotrachelus nenuphar (adult)	Topical	LC$_{50}$	14 ppm	By surface wetting in H$_2$O suspension.	2864
Conotrachelus nenuphar (")	Residue	MER*	34 mg/100 cm^2	*=Minimum Effective Residue.	2864
Diataraxia oleracea (larva 0.32 g wgt)	or	LD$_{50}$	2.6μg/larva	Settling tower; leaf method.	3245
Diataraxia oleracea (" 0.42 g ")	or	LD$_{50}$	3.4μg/larva	" .	3245
Diataraxia oleracea (" 0.56 g ")	or	LD$_{50}$	4.6μg/larva	" .	3245
Ephestia kühniella (larva 1 cm length)	Contact Spray	LC$_{50}$	0.21 g/l	Emulsions applied in dusting tower.	775
Ephestia kühniella	or	LD$_{50}$	0.01μg/insect; 1 mg/k		1119
Galleria mellonella	or	LD$_{50}$	125μg/g	"Enteral route."	206
Galleria mellonella	or	LD$_{95}$	532μg/g	" .	206
Galleria mellonella	Topical	LD$_{50}$	2215μg/g		206
Galleria mellonella	Topical	LD$_{95}$	24,200μg/g		206
Galleria mellonella	inj	LD$_{50}$	91.1μg/g	"Parenteral route."	206
Galleria mellonella	inj	LD$_{95}$	3706μg/g	" .	206
Galleria mellonella	Fumig	LD$_{50}$	>57,600 sec. exp. time	Exceeds the measurable dose.	206
Melanoplus differentialis (1st, 2nd instar)	Contact Spray	LD$_{50}$	0.05 lbs/acre	As contact emulsion sprays.	1102
Melanoplus differentialis (adult)	Topical	LD$_{50}$	0.7; 0.8μg/g	Tech. parathion.	3267
Melanoplus differentialis (")	or	LD$_{50}$	6.0; 8.9μg/g	As a deposit on leaves.	3267
Musca domestica (adult)	Topical	LC$_{50}$	0.032 g/l	As contact emulsion; dusting tower.	775
Musca domestica (")	or	LD$_{50}$	0.01μg/fly; 0.5μg/g		1119
Musca domestica (")	Contact Spray	LC$_{50}$	0.03 ± .003 mg/cc	17 ± 2 times as toxic as HETP.	1164
Musca domestica (")	Topical	LD$_{50}$ 24 hr.	1.4 μg/g	Methyl parathion 1.3; isopropyl parathion.48.	2247
Musca domestica (")	Contact Spray	LC$_{50}$ 24 hr.	0.02 mg/cc	Turntable application, Peet-Grady.	2033
Musca domestica (")	Topical	LD$_{50}$ 24 hr.	0.015μg/fly	At 60°F; laboratory, DDT-non R.	371
Musca domestica (")	Topical	LD$_{50}$ 24 hr.	0.020μg/fly	" ; Bellflower, DDT-R strain.	371
Musca domestica (")	Topical	LD$_{50}$ 24 hr.	0.023μg/fly	" ; Pollard, " .	371
Musca domestica ♀ (adult)	Topical	LD$_{50}$	0.015-0.023μg/fly	Laboratory strain.	1761
Musca domestica ♀ (")	Topical	LD$_{50}$	0.06μg/fly	J74 field strain; 3 yrs. selection vs. parathion.	1761
Musca domestica ♀ (")	Topical	LD$_{50}$	0.09μg/fly	J79 " "	1761
Musca domestica ♀ (")	Topical	LD$_{50}$	0.03μg/fly	Z98 " 1 season exp to Diazinon. 1 season exp to Bayer 21/99.	1761
Musca domestica ♀ (")	Topical	LD$_{50}$	0.05μg/fly	Z127 Exposure 1 season to parathion. 1 season to Diazinon. 1 season to Bayer 21/199.	1761
Musca domestica ♀ (")	Topical	LD$_{50}$	0.05μg/fly	Z129 " "	1761
Musca domestica ♀ (")	Topical	LD$_{50}$	0.06μg/fly	Z149 " 2 seasons to parathion. 1 season to Diazinon. 1 season to Bayer 21/199.	1761
Musca domestica ♀ (")	Topical	LD$_{50}$	0.04μg/fly	F151 " 2 seasons to diazinon.	1761
Myzus persicae	Contact Spray	LC$_{50}$	0.021; 0.0125 g/l	Emulsion; applied in dusting tower.	775
Oncopeltus fasciatus	Topical	LD$_{50}$	47μg/g		206
Oncopeltus fasciatus	Topical	LD$_{95}$	140μg/g		206
Oncopeltus fasciatus	inj	LD$_{50}$	8.39μg/g	Parenteral administration.	206
Oncopeltus fasciatus	inj	LD$_{95}$	28.3μg/g	"	206
Periplaneta americana ♂	Topical	LD$_{50}$ 120 hr.	0.9μg/g)	Para-oxon = 0.7.	2244
Periplaneta americana ♀	Topical	LD$_{50}$ 120 hr.	1.5μg/g	" = 0.8.	2244
Periplaneta americana ♂	inj	LD$_{50}$ 120 hr.	0.9μg/g	" = 0.6.	2244
Periplaneta americana ♀	inj	LD$_{50}$ 120 hr.	1.0μg/g	" = 0.7.	2244
Plusia gamma	or	LD$_{50}$	2.5μg/insect; 7.5μg/g		1119
Popillia japonica	Topical	LD$_{50}$	3.3μg/g		206
Popillia japonica	Topical	LD$_{95}$	27.8μg/g		206
Popillia japonica	or	LD$_{50}$	4.51μg/g	Enteral administration.	206
Popillia japonica	or	LD$_{95}$	23.0μg/g	"	206
Popillia japonica	inj	LD$_{50}$	0.448μg/g	Parenteral administration.	206
Popillia japonica	inj	LD$_{95}$	5.79μg/g	"	206
Protoparce sexta (larva)	or	LD$_{50}$	15.7μg/larva	5th instar 5.4(4.1-7.5) g wgt.	1306
Protoparce sexta (")	or	LD$_{90}$	54.0μg/larva	" .	1306
Protoparce sexta (")	Topical	LD$_{50}$	52.0μg/larva	" .	1306
Protoparce sexta (")	Topical	LD$_{90}$	183.0μg/larva	" .	1306
Protoparce sexta (")	Topical	LD$_{50}$	9.9μg/larva	3rd, 4th instar 2.5(1.2-4.0)g wgt.	1306
Protoparce sexta (")	Topical	LD$_{90}$	64.0μg/larva	"	1306
Protoparce sexta (")	Topical	LD$_{50}$	2.8μg/larva	2nd, 3rd instar 0.9(0.6-1.1)g wgt.	1306
Protoparce sexta (")	Topical	LD$_{90}$	12.3μg/larva	"	1306
Rhagoletis cingulata (1 day adult)	Contact Mist	LC$_{50}$ 24 hr.	0.007%	At 75°F, aqueous emuls. mist; spray chamber.	1706
Rhagoletis cingulata (")	"	LC$_{95}$ 24 hr.	0.038%	" " "	1706
Sitophilus granarius (adult)	Contact Spray	LC$_{50}$	0.044; 0.031 g/l	Dusting tower application.	775
Tenebrio molitor (larva 2-2.5 cm)	Contact Spray	LC$_{50}$	0.165 g/l	" .	775
Tribolium confusum (adult)	Contact Spray	LC$_{50}$	0.031; 0.046 g/l	" .	775
T. bimaculatus	Contact Spray	LC$_{50}$	0.02 g/l	" .	775
T. bimaculatus	Topical	LC$_{50}$	0.013 g/100 cc	Emulsion; settling tower application.	904
T. bimaculatus	Topical	LC$_{50}$	0.0048 g/100 cc	Suspension; settling tower; on bean leaves.	904
T. bimaculatus	Topical	LC$_{50}$	0.0068 g/100 cc	Emulsion; sprayer applied; on avocado leaf.	904
T. bimaculatus	Topical	LC$_{50}$	0.0051 g/100 cc	Suspension; " ; "	904
T. bimaculatus	Residue	LC$_{50}$	0.0095 g/100 cc	Emulsion; settling tower; mites placed on treated leaves.	904
T. bimaculatus	Residue	LC$_{50}$	0.0072 g/100 cc	Suspension; settl. tower; mites placed on treated bean leaves.	904
T. bimaculatus	Residue	LC$_{50}$	0.013 g/100 cc	Emulsion; settl. tower; mites avocado leaves.	904
T. bimaculatus	Residue	LC$_{50}$	0.0081 g/100 cc	Suspension; " " .	904
T. bimaculatus	Residue	LC$_{50}$	0.0012 g/100 cc	Emulsion; sprayer " " .	904
T. bimaculatus	Residue	LC$_{50}$	0.0004 g/100 cc	Suspension; " " " .	904
T. bimaculatus	Topical, + Residual	LC$_{50}$	0.003 g/100 cc	Settling tower; Emulsion; on bean leaves.	904
T. bimaculatus	"	LC$_{50}$	0.0017 g/100 cc	" ; Suspension; "	904
T. bimaculatus	"	LC$_{50}$	0.0075 g/100 cc	" ; Emulsion; on avocado leaves.	904
T. bimaculatus	"	LC$_{50}$	0.0061 g/100 cc	" ; Suspension; " .	904

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
T. bimaculatus	Topical + Residual	LC$_{50}$	0.00076 g/100 cc	Sprayer; Emulsion; on avocado leaves.	904
T. bimaculatus	"	LC$_{50}$	0.00031 g/100 cc	" ; Suspension; "	904
T. bimaculatus (adult)	Residual	LC$_{50}$ 48 hr.	0.0056 g/100 cc	Settling tower; Emulsion; on treated bean leaves.	905
T. bimaculatus (")	Residual	LC$_{50}$ 48 hr.	0.0045 g/100 cc	" ; Wett. pwdr; "	905
T. bimaculatus (larva)	Residual	LC$_{50}$ 48 hr.	0.013 g/100 cc	" ; Emulsion; "	905
T. bimaculatus (")	Residual	LC$_{50}$ 48 hr.	0.010 g/100 cc	" ; Wett. pwdr.; "	905
T. bimaculatus (egg)	Residual	LC$_{50}$ 48 hr.	0.19 g/100 cc	" ; Emulsion; "	905
T. bimaculatus (")	Residual	LC$_{50}$ 48 hr.	0.37 g/100 cc	" ; Wett. pwdr.; "	905
T. bimaculatus (adult)	Residual	LC$_{50}$ 48 hr.	0.021 g/100 cc	" ; Emulsion; mites on leaf surface opposite to treated surface.	905
T. bimaculatus (")	Residual	LC$_{50}$ 48 hr.	0.027 g/100 cc	Settling tower; Wett. pwdr; mites on leaf surface opposite to treated surface.	905
T. bimaculatus (♀)	Topical	LD$_{50}$	1.8 μg/mite (??)	(90 mg/k).	1121
T. bimaculatus (♀)	Topical	LD$_{100}$	4.0 μg/mite (??)	(200 mg/k).	1121
Paratetranychus citri	Contact Spray	LC$_{50}$ 24 hr.	0.0001% (conc.)	95% tech. parathion.	2230
Heliothrips haemorrhoidalis	Contact Spray	LC$_{50}$ 24 hr.	0.0001% (conc.)	"	2230

(1) Residual toxicity of parathion for Tetranychus bimaculatus; tested as a 15% wettable powder at 2 Lbs/100 gal. on Phaseolus coccineus leaves; >760 to ca. 1000 mites examined in each test: 117

Days Between Spraying And Infesting Plants	% Mortality After	
	7 days	14 days
1	90.5	99.8
2	89.7	99.2
3	91.0	94.4
4	80.5	91.7
5	75.5	84.5
6	89.2	98.0
7	57.3	54.3
10	73.3	51.6
14	35.3	19.5
Control	1.9	4.1

Eggs placed on sprayed foliage hatch but most of the newly emerged mites are destroyed when placed on residues up to ca. 7 days old.

b) Comparative toxicity, parathion and other compounds: (For comparative toxicity data for acarines, consult the tabulations in the section titled Miticides or Acaricides.)

(1) Comparative toxicity vs. Aëdes aegypti larvae: 1427

LD$_{100}$ (ppm) For									
Parathion	Aldrin	Heptachlor	Dieldrin	Chlordane	Lindane	DDT	Methoxychlor	DDD	Toxaphene
0.0006	0.0078	0.016	0.016	0.016	0.031	0.0625	0.0625	0.0625	0.0625

(2) Vs. Anasa tristis; laboratory tests; by topical application in acetone solution: 3376

Substance	% Mortality At 72 Hrs. With				
	32 μg/g	64 μg/g	128 μg/g	256 μg/g	512 μg/g
Parathion	100	100	100	100	100
Lindane	83.3	100	100	100	100
Aldrin	—	93.3	100	100	100
Endrin	—	—	100	100	100
EPN®	—	—	100	100	100
Heptachlor	—	83.3	90	100	100
Isodrin	—	—	90	100	100
Dieldrin	—	—	70	100	100
Chlordane	—	—	36.7	80	90
Toxaphene®	—	—	16.7	66.7	82
"	—	—	20	30	76.7

Mortality after 30 minutes exposure to surfaces treated 7 days before test at 100 mg/ft^2:

Substance	% Mortality In			
	24 hrs.	48 hrs.	72 hrs.	96 hrs.
Parathion	10	10	20	40
Dieldrin	30	80	80	100
Lindane	10	20	20	20
Heptachlor	0	10	20	20
Aldrin	0	0	0	0

Rates of action at the lowest topical dosages yielding a 90% (or higher) mortality in 72 hours:

Substance	(μg/g)	% Mortality In 12 hrs.	24 hrs.	48 hrs.	72 hrs.
Parathion	6	3.3	33.3	76.7	90
Lindane	64	—	80	100	100
Aldrin	64	—	23.3	76.7	93.3
Endrin	128	6.7	20	80.7	100
EPN®	128	10	26.7	76.7	100
Heptachlor	128	10	50	80	90
Isodrin	128	0	10	63.3	90
Dieldrin	256	0	70	96.7	100
Chlordane	512	—	6.7	73.3	90

(3) Vs. Anopheles quadrimaculatus larvae (4th instar) in laboratory and field tests and Anopheles crucians in field tests. 1766

	Laboratory Tests % Mortality (A. quadrimaculatus) 48 Hrs. At (ppm)									Field Tests Vs. A. quadrimaculatus And A. crucians % Mortality 24 Hrs. At (Lbs/acre)							
Insecticide	0.1	.05	.025	.01	.005	.0025	.001	.0005	.25	.1	.05	.025	.01	.005	.0025	.001
Parathion	100	——	——	——	——	96	56	34	—	—	97	97	92	99	88	—
Sulfotepp	100	——	——	——	——	——	74	34	—	85	72	73	63	53	30	—
EPN®	100	——	——	——	——	96	32	—	—	—	95	96	96	95	92	91
Methyl parathion	100	——	——	——	——	67	—	—	—	100	98	83	69	51	50	—
*	100	——	——	96	86	62	62	64	—	99	72	78	49	30	—	—
Malathion	100	——	96	80	80	60	40	24	90	78	79	68	60	—	—	—
**	100	——	——	——	70	80	4	—	—	99	80	88	75	70	69	71
Diazinon	100	——	——	——	36	20	—	—	—	97	97	79	58	65	55	53
Para-oxon	100	——	——	82	50	—	—	—	—	90	77	54	46	45	49	31
***	100	——	——	64	46	24	—	—	—	—	98	98	99	96	91	84
Chlorthion®	100	——	88	76	44	—	—	—	100	99	82	73	57	50	—	—
Potasan®	100	98	56	30	5	—	—	—	—	77	59	72	52	—	—	—
****	100	94	58	26	—	—	—	—	—	—	78	64	75	74	45	35
NPD	94	—	62	30	—	—	—	—	100	97	84	87	79	—	—	—
DDT				100	94	49	24	—	—	—	99	98	99	98	95	92

*O,O-dimethyl O(2-chloro-4-nitrophenyl) thiophosphate; **Ethyl o-nitrophenyl thionobenzenephosphonate; ***O,O-dimethyl O(3-chloro-4-methylumbelliferone) thiophosphate; ****O,O-diethyl O-piperonyl thiophosphate.

(4) Vs. Cirphis unipuncta (larvae): 3268

Insecticide	LD$_{50}$ (μg/g) Topical	Ratio	LD$_{50}$ (μg/g) Oral	Ratio	Ratio LD$_{50}$ to LD$_{99}$ Topical	Oral
Parathion*	3.7	1.0 (standard)	2.5	1.0	3.4	8.5
DDT	193	52.2	45.7	18.3	4.7	22.8
Chlordane	117.5	31.6	78.2	31.3	4.9	4.7
Toxaphene®	56.2	15.2	34.1	13.6	4.7	2.9
Lindane	28.1	7.6	27.9	11.2	3.2	5.1
Aldrin	19.8	5.4	11.4	4.6	3.7	24.7
Dilan	8.8	2.4	11.5	4.6	5.4	5.0
Dieldrin	8.3	2.2	4.6	1.8	3.1	3.8

*Yielded most rapid kill, followed (in order) by dilan, lindane, DDT.

(5) Vs. Conotrachelus nenuphar (adult):

Insecticide	Topical* LC$_{50}$ (ppm)	Ratio To Parathion	Field Concentration (ppm)	Minimum Effective Residue (mg/100 cm^2)	Ratio To Parathion
Parathion	14	1	360	34	1
EPN®	32	2.3:1	390	68	2:1
Dieldrin	104	7.4:1	300	71	2.1:1
Methoxychlor	4000	285.7:1	1800	865	25.4:1

*By dipping the insect in insecticides in water suspension.

(6) Vs. Diataraxia oleracea (final larval instar) administered as oral (stomach) poisons (on leaves treated in the settling tower) to larvae of various body weights. 3245

Insecticide	LD$_{50}$ (μg/larva) For Larvae Of Stated Weight 0.32 g wgt.	0.42 g wgt.	0.56 g wgt.
Parathion*	2.6	3.4	4.6
Lead arsenate	66	78	91

(6) Vs. Diataraxia oleracea (final larval instar) administered as oral (stomach) poisons (on leaves treated in the settling tower) to larvae of various body weights. 3245

Insecticide	LD50 (μg/larva) For Larvae Of Stated Weight		
	0.32 g wgt.	0.42 g wgt.	0.56 g wgt.
TEPP	43	69	1.12
Lindane	13	26	59
DDT	4.5	12	33

*Dosage is linearly related to body weight.

(7) Vs. Melanoplus differentialis (adult): 3267,1102

Insecticide	Topical LD50 (μg/g)	Oral LD50 (μg/g)	(Vs. 1st And 2nd Instar) LD50 (Lbs/acre) As Contact Emulsion Sprays
Parathion (tech.)	0.7; 0.8	6.0; 8.9	0.05
TEPP	4.4	—	—
HETP	18.4	—	—
Dieldrin	1.4	3.7	0.03
Aldrin	1.8	2.3	0.04
Heptachlor	2.6; 1.6	6.0; 4.4	—
Lindane	1.6; 3.4	6.6; 6.7	0.08**
Chlordane	16.3; 9.8	21.8; 12.0	0.49
Toxaphene®	73.9;61.0	75.0; 91.5	0.91
DDT	9380.0	2579.0;1170.0*	—

*As a colloidal suspension applied directly to mouth parts.
**BHC = 0.04

(8) Vs. Musca domestica (adult) as acetone-kerosene sprays 1 to 1: 1164

Insecticide	Concentration (mg/cc)	% Mean Mortality (1 Day)	Mean Concentration For 50% Mortality (mg/cc)	Relative Toxicity At LC50
Parathion	0.079	100	0.03 ± .003	17 ± 2
"	.039	71		
	.026	47		
	.020	11		
HETP	.64	58	0.52 ± .05	1.0 (standard)
"	.32	33		
	.16	3		
TEPP	.3	100	0.095 ± .01	5.5 ± 0.7
	.15	70		
"	.074	43		
	.037	10		
Pyrethrins (standard)	2	70	1.2 ± .14	0.43
"	1	45		

(9) Vs. Musca domestica: 2033,2247

Insecticide	LC50 As Contact Spray* (50% kill At 24 Hrs) (mg/cc)	"Knockdown" In 10 Minutes At LC50 (%)	LD50 (Topical) 24 Hrs. (μg/g)
Parathion	0.02	0	1.4
Methyl parathion	.025	0	1.3
Isopropyl parathion	—	—	4.8
Malathion	.48	0	27.0
EPN®	—	—	2.0
TEPP	.069	ca. 70	—
Tetrapropyl dithiopyrophosphate	.69	0	—
Isolan	1.15	100	—
Pyrolan	5.5	100	—
Allethrin	1.5	100	—
Dieldrin	.017	0	—
Lindane	.046	0	—
Heptachlor	.052	0	—
Aldrin	.056	0	—
Chlordane	.25	0	—
DDT	.35	0	—
Toxaphene®	.68	0	—
Dilan®	.72	ca. 30	—

*By turntable modification of Peet-Grady Method.

(10) Parathion and Para-oxon vs. Periplaneta americana: 2244

Parathion								Para-oxon							
LD_{50} 120 Hrs. (μg/g) By				Time (Min.) For				LD_{50} 120 Hrs. (μg/g) By				Time (Min.) For			
Topical		Injection		50% Paralysis At		100% Paralysis At		Topical		Injection		50% Paralysis At		100% Paralysis At	
♂	♀	♂	♀	5 μg/g	50 μg/g	5 μg/g	50 μg/g	♂	♀	♂	♀	5 μg/g	50 μg/g	5 μg/g	50 μg/g
0.9	1.5	0.9	1.0	65	35	80	60	0.7	0.8	0.6	0.7	15	1-2	25	5

(11) Parathion and derivatives vs. Apis mellifera (adult worker) and Musca domestica (adult): 2244

Compound	LD_{50} (μg/g) For		ID_{50} For Brain Cholinesterase Of	
	Apis	Musca	Apis	Musca
Parathion	3.5	0.9	1×10^{-6} M	4.5×10^{-7} M
Para-oxon	0.6	0.55	1.9×10^{-8} M	2.6×10^{-8} M
Diisopropyl parathion	>1000	4.2	1.4×10^{-2} M	2×10^{-5} M

(12) Vs. Protoparce sexta (larva): S = small larvae 0.9(.6-1.1)g 2,3 instar 1306
M = medium larvae 2.5(1.2-4.0)g 3,4 instar
L = large larvae 5.4(4.1-7.5)g 5 instar

Insecticide	LD_{50} (Topical) (μg/larva)			LD_{90} (Topical) μg/larva			LD_{50} (oral) μg/larva	LD_{90} (or) μg/larva
	L	M	S	L	M	S	L	L
Parathion	52	9.9	2.8	183	64	12.3	15.7	54
Malathion	481	61	23.6	1276	533	92	365	1,621
Endrin	42	2.9	0.51	219	6.3	6.3	9.9	49
Isodrin	87	7.6	3	490	29	56	15.3	138
Lindane	206	—	—	1235	—	—	209	398
Dieldrin	482	—	—	2559	—	—	—	—
Aldrin	487	—	—	1359	—	—	—	—
Heptachlor	1058	—	—	4005	—	—	—	—
Toxaphene®	1363	32	30	5778	138	112	143	6,025
DDD	2622	376	37	9813	2620	367	878	3,192
DDT	≫4000	2334	366	—	9887	1342	4416	28,040

(13) Vs. Sphaenarium purpurascens on corn; field tests: 307

Insecticide	Concentration And Form	Lbs/Acre (Active Ingredient)	% Mortality After	
			12 Hrs.	24 Hrs.
Parathion	0.5% Dust	0.16	43.6 (36-51)	69.4 (61-80)
"	1.0% "	.35	66.8 (59-80)	76 (69-84)
Dieldrin	1.0% "	.35	74.2 (68-80)	98.2 (96-100)
"	2.5% "	.88	89.8 (87-93)	99.8 (99-100)
Aldrin	1.0% "	.32	77.8 (69-88)	97.8 (95-100)
"	2.5% "	.82	88.6 (83-96)	99.6 (99-100)
BHC	1.0% "	.36	86.6 (78-92)	94.2 (90-97)
"	2.5% "	.85	93 (89-98)	97 (93-100)
Isodrin	0.5% Spray	.43	83.2 (81-92)	91.4 (80-96)
Toxaphene®	5.0% Dust	1.74	26.8 (18-36)	53 (46-60)
"	10.0% "	3.6	40.4 (36-47)	61.4 (55-59)
Chlordane	2.5% "	.95	32 (27-39)	46.6 (41-54)
"	5.0% "	1.8	49.6 (39-62)	63.8 (50-77)
Endrin	0.5% Spray	.36	32.8 (24-40)	47.6 (43-59)

(14) Vs. various adult insects; parathion, dimetan, pyrolan: 1286

Insect	LD_{50} (Oral) Of					
	Parathion		Dimetan		Pyrolan	
	μg/insect	μg/g	μg/insect	μg/g	μg/insect	μg/g
Plusia gamma	2.5	7.5	10	30	8	24
Apis mellifera	0.1	1.0	11.5	13	1.0-1.5	13
Musca domestica	0.01	0.5	.05-.07	3.2	0.05-0.07	3.2
Ephestia kühniella	0.01	1.0	0.005	0.5	.005	0.5
Aphis rumicis	0.0005	0.8	0.0005	0.8	.0005	0.8

(15) Parathion and malathion vs. various insects; contact sprays from concentrates in white spirit, dusting tower application: 775

Insect	Parathion LC_{50} (g/l)	Malathion LC_{50} (g/l)	$\frac{\text{Parathion}}{\text{Malathion}}$ x 100
Musca domestica (adult)	0.032	0.74	4.3
Sitophilus granarius (adult)	.044;.031	.092;.088	47.8;45.3
Tenebrio molitor (larva, 2-2.5 cm.)	.165	>1.6	<10
Tribolium confusum (adult)	.031;.046	.42;.53	7.2;8.7
Ephestia kühniella (larva, 1 cm.)	.21	>4	< 5
Chaitophorus populi	.008	.022	36.4
Myzus persicae	.021;.0125	.098;.03	21.4;41
Tetranychus bimaculatus	.02	.049	41

(16) Vs. Tetranychus bimaculatus; parathion and other acaricides; residual effectives against mites placed on bean and avocado leaves, treated by the settling tower method: 904

Substance	Formulation	LC_{50} g/100 cc On	
		Bean Leaves	Avocado Leaves
Parathion	Emulsion	0.0095	0.013
"	Suspension	0.0072	0.0081
Sulphenone®	Emulsion	0.25	0.54
"	Suspension	0.45	0.60
Aramite®	Emulsion	0.0031	0.012
"	Suspension	0.0035	0.014

Effectiveness as emulsions in killing adult mites on leaf surfaces opposite the treated surfaces; sprays: 904

Substance	Concentration (%)	Leaf Type	% Mortality (net)	
			At 48 Hrs.	At 96 Hrs.
Parathion	0.03	Bean	91.5	95.4
"	0.03	"	100	100
"	0.12	Grapefruit	77	100
"	0.12	"	96.7	100
"	0.12	Avocado	52.8	82.5
"	0.12	"	85.3	100
Aramite®	0.12	Bean	49.4	98.2
"	0.12	"	82.5	100
"	0.12	Grapefruit	13.1	34.2
"	0.12	"	60.8	96.1
"	0.12	Avocado	0	26.0
"	0.12	"	0	55.3

(17) Parathion vs. Tetranychus bimaculatus by various methods; topical (=T) treatment then transfer to untreated leaves; Residue (R) = mites not directly treated but placed on treated leaves; TR = topical treatment with mites remaining on the treated leaves: 904

Treatment Method	Leaf	Formulation	LC_{50} (g/100 cc)		
			T	R	TR
Parathion					
Settling Tower	Bean	Emulsion	0.013	0.0095	0.0030
"	Bean	Suspension	.0048	.0072	.0017
"	Avocado	Emulsion	—	.013	.0075
"	Avocado	Suspension	—	.0081	.0061
Sprayer	Avocado	Emulsion	.0068	.0012	.00076
"	Avocado	Suspension	.0051	.0004	.00031
Aramite®					
Settling Tower	Bean	Emulsion	0.014	0.0031	0.0018
"	"	Suspension	.038	.0035	.0023
"	Avocado	Emulsion	—	.012	.0089
"	"	Suspension	—	.014	.0088
Sprayer	"	Emulsion	.0031	.0015	.0006
"	"	Suspension	.0056	.0033	.002
Sulphenone®					
Settling Tower	Bean	Emulsion	0.93	0.25	0.085
"	"	Suspension	5.4	.45	.26
"	Avocado	Emulsion	—	.54	.29
"	"	Suspension	—	.6	.48
Sprayer	"	Emulsion	0.12	.11	.037
"	"	Suspension	.32	.28	.11

(18) Vs. Haematopinus eurysternus; as spot treatments using emulsion concentrate and wettable powder formulations: 2862

Insecticide	Concentration (%)	% Mortality 24, 48 Hrs.	Weeks Effective
Parathion	0.05	100	3
"	.01	100	3
"	.005	25	0
Malathion	.5	100	2
"	.05	100	1
Chlorthion®	.25	100	1
Dipterex®	.25	100	1
"	.1	100	0
Bayer 21/199	.25	100	2
"	.2	100	2
"	.1	100	1
"	.05	100	1
Diazinon	.25	100	2
"	.1	100	2
"	.05	100	1
"	.01	95	1
"	.005	25	1
"	.002	5	1
Pirazinon	.25	100	3
EPN®	0.05	100	1
"	.01	100	1
"	.005	100	1
"	.002	25	0
Tetrapropyl dithiopyrophosphate	.05	100	1

(19) Vs. Psylla pyri; as autumn sprays applied in central France in 1st half of October by motor spraying at pressure of 12 k/cm^2; entomophagous and predatory insects were unharmed: 2275

Material Tested	Formulation Conc. (Active Ingredient) (%)	Dilution %	Coefficient Of Efficacity
Parathion	Emulsion 3%	0.75	100
"	" 4%	0.35	98.7
"	1.5% + white summer oil	1.0	96.1
" "	1.5% + summer oil + Suspension 3%	0.35	100
White Summer Oil	80%	1.5	14.9
" + nicotine	73%: 11.5%	0.75	31.9
" + rotenone	60%: 0.9%	1.0	56.6
DDT	Emulsion 20%	0.5	27.7
TEPP	13%	0.15	12.8
BHC	12% Gamma isomer	0.3	98.7

(20) Vs. Macrosiphum pisi on Vicia faba; speed of toxic action as dusts (in talc) applied by dusting tower method: 520

Insecticide	Concentration (%)	Temperature (°F)	Time (Hrs:Min) For	
			50% Kill	98% Kill
Parathion	1	70	1:8	1:43
"	2	70	1:21	1:53
DDT	5	72	0:57	1:45
Lindane	1	72	0:56	1:54
Rotenone	5	72	0:47	1:23
TEPP	0.18	74	0:20	0:56
Nicotine	1	72	0:15	1:12
"	3	72	0:12	0:50
Toxaphene®	5	72	13:20	19:1
Chlordane	5	72	9:24	18:8
EPN®	0.86	74	5:26	8:6
Dieldrin	1	75	4:7	6:43
Aldrin	1	75	3:44	7:32
DDD	5	72	2:34	4:35
Methoxychlor	10	75	2:1	5:34
Talc (alone)	100	67-72	13:28	23:51

(21) Vs. the overwintering eggs of Aphis pomi and Operophthera brumata subjected to 10 second immersions (100 - >300/trial) at the stated concentrations: 899

Compound	% Mortality At Concentration Of 0.2% (Aphis pomi)	 0.05% 	 0.2% (Operophthera brumata)	 0.05%
Parathion	100	78.6	95.4	90.8
Para-oxon	99.6	100	7.8	4.4
Triethyl phosphate	1.4	0	3.1	7.1
Triphenyl phosphate	14.1	0	8.0	6.4
Tri-o-tolyl phosphate	0	7.1	5.8	7.9
Triphenyl phosphine	13.9	5.1	3.4	3.6
HETP	7.4	1.1	6.2	3.7
Diethyl acetyl phosphate	5.7	8.4	8.7	1.3
Diphenylethyl thionophosphate	0	8.1	8.5	4.8
p-Nitrophenyl dichlorothionophosphonite	40.4	10.3	—	10.2
Diphenyl chlorothionphosphonate	25.9	4.9	4.0	3.0
Tri-(p-nitrophenyl) thionophosphate	5.3	0.6	1.9	4.3
Tri-(p-chlorophenyl) "	15.7	13.0	1.6	1.9
TEPP	3.3	2.6	7.2	6.5
Diethyl 1-carbethoxyprop-1-en-z-yl phosphate	100	86.3	18.3	2.3
Phenyl diethyl phosphate	59.3	2.9	2.5	3.3
p-Chlorophenyl diethyl phosphate	93.9	14.6	2.5	2.2
Phenyl diethyl thionophosphate	39.9	3.7	1.7	1.6
Triphenyl thionophosphate	19.0	23.7	0	3.7
Tetraethyl dithionopyrophosphate	100	54.6	24.0	4.6
Tetraethyl monothionopyrophosphate	12.0	2.4	19.0	1.6
Pyrophosphoric tetrakis dimethylamide	9.0	0	1.4	0
Control Hatch	69.9%		97.1%	

(22) Vs. Brachycaudis helichrysi, Phorodon humuli and Aphis pomi; as sprays: 899

Insecticide	B. helichrysi Concentration (%)	 Aphis/100 Leaves Before Spray	 After Spray	P. humuli Concentration (%)	 Aphis/100 Leaves Before Spray	 After Spray	A. pomi Concentration (%)	 Colonies/Plot Before Spray	 7 Days After Spray	 24 Days After Spray
Parathion	0.05	1445	10	0.025	2580	5	0.05	35.8	5	14.4
HETP	0.05	2132	40	0.025	3120	53	0.05	36.0	2.8	20.2
Nicotine	0.05	1881	250	0.025	2630	422	0.05	18.4	5	17.4
Control	0	2467	326	0	2740	2267	0	25.8	32.8	22.4

(23) Vs. Aphids, comparative effectiveness: 353

Aphis gossypii	Parathion >nicotine, BHC, Toxaphene® >DDT
Brevicoryne brassicae	Parathion >HETP >nicotine >DDT
Rhopalosiphum pseudobrassicae	Parathion >BHC >nicotine >DDT
Macrosiphum onobrychis	Parathion, HETP, BHC >nicotine, DDT, rotenone
Macrosiphum solanifolii	DDT, BHC >nicotine, rotenone
Myzus persicae	Parathion >HETP >BHC >nicotine >DDT
Eriosoma lanigerum	Parathion >BHC >nicotine >HETP >DDT

c) Parathion and beneficial insects:

(1) For general considerations see Ref. 2650.

(2) Vs. Collops vittatus, Hippodamia convergens and Coleomegilla maculata; treated with dusts (adult insects placed on plants treated previously by vacuum dusting): 1404

Insecticide	Concentration (%)	% Mortality 24 Hrs. Of Collops	 Hippodamia	 Coleomegilla
Parathion	2	65	78	98
Malathion	5	47	90	100
Chlorthion®	5	64	82	100
Diazinon	4	37	66	100
DDT	8	38	6	32
Perthane	5	23	6	12
Strobane®	5	10	18	12
Heptachlor	2.5	41	30	38
Toxaphene®	10	32	12	36
Endrin	1	27	10	18
Dieldrin	2	36	4	24
Control	—	11	4	0
Lowest Sig. Difference 5% level		20	24	26

(3) Vs. Apis mellifera; (also consult the section on Bees and Insecticides):

(a) Exceedingly toxic and hazardous for bees, the lethal effects continuing 2-4 days from the time of exposure. High toxicity orally and by contact, with a high fumigant effect. Equals (for bees) the hazard of calcium arsenate. Treatment of blossoming alfalfa fields with a 1% dust has yielded a 40% mortality among the bee field-force. The oral LD_{50} for an adult worker is reported as 0.07 μg/bee. 3099 3098 1330 909 429,927

(b) As a stomach and contact poison for bees, parathion outstrips in toxicity (in the following order) 1718

TEPP, lindane, dieldrin, aldrin, chlordane, Systox®, BFPO, Toxaphene®, Na salt of 2,4-D, Na salt of MCPA; as a residue only dieldrin, aldrin, and lindane are more toxic than parathion which in its turn is more toxic as a residue than chlordane or Systox®; the same holds in fumigant toxicity.

(c) Intensely more toxic for bees than Schradan (OMPA), both as a stomach and a residual poison. 1719

Parathion (Oral)	
Dose/Bee (mg x 10^{-5})	% Kill 24 Hrs.
70	100
25	85
6	60
3	43
2.5	28
0.5	0

Schradan (Oral)	
Dose/Bee (mg x 10^{-2})	% Kill 24 Hrs.
25	100
20	85
15	64
10	47
8	17
5	10

(d)

	Parathion (Contact Spray)		Schradan (Contact Spray)	
	mg/cm² x 10^{-5}	% Kill 24 Hrs.	mg/cm² x 10^{-3}	% Kill 24 Hrs.
	64	100	65	35
	51	82.5	31	25
	42	70	6.5	22
	36	42.5	3.1	0
	25	20	—	—
	5	0	—	—
On dry films	0.06	100	0.06	7

(e) As stomach poison vs. bees; parathion and other compounds; as contact sprays: 1718

Insecticide	Contact Sprays			Stomach Poisons		
	Dosage (mg/cm² x 10^{-5}) To Give Kills Of			Dosage (mg x 10^{-5}) To Give Kills Of		
	20%	50%	90%	20%	50%	90%
Parathion	25.7	35.4	57.4	1.8	4.0	14.4
TEPP	35.8	44.5	62.1	5.2	6.5	9.3
Dieldrin	38.6	57.5	105.2	22.3	26.9	35.4
Aldrin	32.7	56.2	127.4	18.1	23.9	36.5
Lindane	77.2	85.1	98.6	2.6	7.9	34.6
Chlordane	380.2	500.0	758.0	83.1	112.2	173.0
Systox®	432.1	512.3	661.9	125.5	147.8	188.4
Dimefox®	1652.0	2317.0	3864.0	125.0	190.5	350.6
Toxaphene®	3673.0	4467.0	5998.0	2512.0	3981.0	8017.0

(f) Bees in contact for 1 hour with residual films: 1718

Insecticide	% Kill 24 Hrs.	Dry Film μg/cm²	Field Average Dose μg/cm²	Ounces/Acre
Parathion	90	0.54	1.4	2
"	10	0.18	—	—
Dieldrin	90	0.09	1.4	2
"	10	0.04	—	—
Aldrin	75	0.09	1.4	2
"	0	0.04	—	—
Lindane	100	0.28	2.8	4
"	0	0.074	—	—
Chlordane	100	3.4	11.2	16
"	12	0.9	—	—
Systox®	50	10.0	—	—
"	22	6.8	—	—
TEPP	8	0.22	5.6	8
Toxaphene®	9	110	16.8	24
"	0	40	—	—
Dimefox®	0	50	—	—

(g) Toxic effects of vapors from residual films; bees exposed for 1 hour to the vapors: 1718

Insecticide	% Kill 24 Hrs.	Dry Films (μg/cm^2)
Parathion	100	5.0
"	0	2.8
Dieldrin	100	.280
"	0	.074
Lindane	100	.44
"	0	.28
Aldrin	100	.74
"	0	.074
Chlordane	100	3.7
"	0	.37
Toxaphene®	0	70.0
TEPP	0	5.5
Systox®	0	18.5
Dimefox®	0	74.0

(h) Parathion is severely toxic to Metaphycus luteolus, a highly useful parasite of Coccus hesperidium 198
in citrus groves. Treated orange groves remained lethal to the parasite for from 6 weeks to 3 945
months or more, with consequent upsurge in soft brown scale (C. hesperidium) numbers.

d) Systemic action of parathion treated plants:

(1) Parathion is not in general considered to be one of the economically very useful systemic insecticides. 2231
Parathion has, however, in certain situations been shown to exert a systemic effect via the transpiration 2651
stream of treated plants. Parathion is far surpassed in systemic action by para-oxon which is 100 2773
times as soluble in water as is parathion. 353

(2) Systemic action vs. newly hatched European corn borer larvae on parts of Zea mays plants grown in parathion treated soils has been reported. 2564

(3) In greenhouse tests parathion water wettable powder was shown to be translocated from the treated soil to nasturtium, bean and squash plants grown from seed, and potato plants developed from tubers in such soils, in sufficient amounts to kill various insects placed on such plants, for example Aphis rumicis and Epilachna varivestis. Application to the soil could be made at the time of (and prior to) planting. 2g/500 g soil (dry weight) gave 100% kills of Aphis rumicis on nasturtiums for 7 weeks (lesser amounts gave lower kills). 100% kills of 3rd instar Epilachna varivestis were recorded on bean plants from the 2nd to 3rd weeks after planting. On potatoes 100% aphid kills were given between the 3rd to 8th weeks after planting at 2 g/500 g soil; kills were greatest on lower and older leaves/and much less at tips. At 2 g per 500 g soil 100% kills of melon aphids were registered on squash at 8 weeks after planting; there were no kills at 0.25 g per 500 g soil. After a relatively brief period of maximum kills systemic action gradually declined to zero. At lower concentrations in soil, aphid reproduction continued unimpaired. 1253

e) Pharmacological, pharmacodynamic, physiological, etc.; insects; (also see the Addendum at the end of this section):

(1) Parathion is characterized as a specifically neurotoxic insect poison by virtue of its in vivo ability 353
potently to inhibit choline esterase(s) known to be present in insect nervous systems, although their 2231
role (as in the case of insect acetylcholine) is disputed and unclear at present. Non-acetylcholine 2043
hydrolyzing esterases (for instance esterases which hydrolyze ethyl butyrate and o-nitrophenyl acetate) are known to be present in insects and to be inhibited by parathion.

(2) Correlation of relative esterase inhibiting action and contact insecticidal activity suggests the interdependence of these properties. 2043

(3) In insects esterases (other than acetylcholine esterase(s) of the nerve system) are deemed important in considering such insecticides as parathion. For example TEPP is a more potent ChE inhibitor than parathion, but parathion is a more potent toxicant for many insects. Many factors are interrelated, including the stability of the insecticide. 2043

(4) Parathion is taken up rapidly into the insect body by all portals of entry (note the high contact toxicity) 166
and transported in the insect by the hemolymph, as parabiosis experiments have shown. The ventral 2231
nerve cord is also associated with parathion transport. The nerve cord is deemed more effective in 2034
transporting the toxic principle which is a metabolite of parathion with the blood playing a secondary 2244
role in its transport. P^{32} labelled parathion has clarified the course of distribution in the insect.
"Knockdown" time for ♀ Periplaneta americana receiving 200 μg/g parathion topically on various areas:

Area	Average "KD" Time (Min.)
Vertex	90.2
Mesosternite	110.0
Second Sternite	120.0
Fourth Sternite	154.3
Sixth Sternite	185.0
Fourth Tergite	212.6

The lethal dose (topical) is almost = to the lethal dose intraparenteral.

(5) Temperature coefficient and parathion action: Musca domestica in contact with residual deposits of parathion shows a greater mortality at 90°F than at 70°F. Thus in contrast with DDT, DDD and methoxychlor and like Toxaphene®, chlordane, aldrin and dieldrin parathion has a positive temperature coefficient. The toxicity of parathion for tetranychid mites increases strongly with temperature. Temperature profoundly affected action on Tetranychus bimaculatus eggs in field experiences; 0.03% sprays at 60°F yielded ca. 15% kills at 80°F ca. 98% kills. 1561 353

(6) Parathion and O_2 consumption: The O_2 consumption increase characteristic of "neurotoxically" poisoned insects is preceded in the case of parathion by a latent period. Blattella, injected with 1µg, showed a steady O_2 consumption of ca. 0.6 mm^3/minute/insect for ca. 150 minutes with the insect passive. Marked increase in O_2 uptake began at 200 minutes and reached a maximum at ca. 250 minutes (2 mm^3/minute/insect). With the onset of paralysis came a steady decline in O_2 uptake; attained the starting O_2 consumption at ca. 700 minutes. 1441

(7) Parathion and heart rate: Increased rate of pulsation of heart in parathion injected Periplaneta, with eventual cessation of beat in systole. Pretreatment with atropine does not protect Periplaneta from parathion. 2421 2244

(8) Parathion and cytochrome oxidase: In vitro systems of Periplaneta coxal muscle cytochrome oxidase as measured by O_2 uptake in Warburg's apparatus, were stimulated at 10^{-5} M but completely inhibited at 10^{-3} M, this last being true of malathion also. 2305

(9) Symptoms and anti-choline esterase activity: Parathion is reported by some to inhibit the choline esterase(s) of Periplaneta in vitro and in vivo and to cause alternation of synaptic block and synaptic facilitation, but to have (in contrast to diisopropyl fluorophosphate, a potent choline esterase inhibitor at low concentrations) no effect on nerve fibers. 2681

(a) Effects of Parathion and TEPP as in vivo inhibitors of Apis mellifera brain choline esterase; 1µg applied to the the thorax; 30 bees per test: 2244

	TEPP		Parathion	
Time After Application	ChE Inhibition Degree (%)	Symptoms	ChE Inhibition Degree (%)	Symptoms
30 minutes	90	Complete "Knockdown"	0	—
60 "	>94	Complete prostration	—	—
2 hours			48	Violent agitation
13 "			65	60-70% "Knockdown," balance lethargic.
18 "			90	Completely prostrate; feeble leg, antenna movements.

(b) Comparative effect of parathion and derivatives on Apis mellifera and Musca domestica: 2244

Compound	LD_{50} µg/g For		ID_{50} For Brain Choline esterase Of	
	Apis	Musca	Apis	Musca
Parathion	3.5	0.9	1 x 10^{-6} M	4.5 x 10^{-7} M
Para-oxon	.6	.55	1.9 x 10^{-8} M	2.6 x 10^{-8} M
p-Nitrophenyl diisopropyl thiophosphate	>1000	4.2	1.4 x 10^{-2} M	2 x 10^{-5} M

(c) Since pure parathion is virtually inactive vs. choline esterase in vitro (as is true of other thionophosphates such as EPN®, malathion, methyl parathion etc.) yet tissue choline esterases in vivo show great inactivation, the substance must be converted in the body to active choline esterase metabolite. Periplaneta tissues, incubated with pure parathion, yield an intensely active choline esterase inhibiting principle, in presence of O_2 and intact tissue. Heating of tissue to 75°C and homogenization, prevent the reaction and indicate it to be enzymatic. Sulfhydryl inactivating substances, iodoacetic acid and chloropicrin also inhibit the reaction strongly as do CN^-, azide, selenite and Hg^{++}. The tissue of the foregut is predominant in degree of conversion of parathion to inhibitor, followed by (in order) midgut, Malpighian tubules, nerve cord, hindgut, fat body; cuticle and muscle effect no conversion. The active anticholinesterase principle (metabolite) is identified chromatographically as para-oxon, and is formed by an oxidation, mediated by an enzyme which removes $S^=$ from the parathion molecule as $SO_4^=$ and replaces it by $O^=$. In the tabulation above the superiority of para-oxon as an insect choline esterase inhibitor is shown. 2243

(10) Overt symptoms of parathion poisoning, Apis mellifera: Topical application: Wild agitation, aggressiveness, cleaning movements; moribund in 30 minutes with the onset of symptoms correlated with degree of brain choline esterase inhibition (vide supra). 909

(11) For a discussion of structure and toxicity of parathion and its isomers and related compounds see Ref. 3365. 3365

(12) Resistance to parathion in insects:

(a) The general problem is discussed succinctly in Refs. 2231, 1597.

(b) Resistant biotypes of Tetranychus bimaculatus have turned up in certain greenhouses. Dosages which gave (as aerosols in methyl chloride) 99.9% kill of the non-resistant biotype(s), yielded but 5% kill of the resistant biotype. 2867

(c) Resistant biotypes of Chromaphis juglandicola, an insect formerly well-controlled by parathion, are reported from certain localities. 2258

(d) A certain degree of "cross-resistance" to parathion is reported for the Ellenville DDT-R biotype of Musca domestica; this cross-resistance to parathion is distinctly less than in the case of certain chlorinated hydrocarbons. 180

(e) Recent data from fly "populations" on Danish farms, where parathion, Diazinon and Bayer 21/199 have been used in animal house fly control, show the selection of resistant or parathion tolerant biotypes: 1761

Strain	Collected (year)	Exposure To Phosphorus Insecticides In The Field				LD₅₀ (Topical) (μg/♀ fly) Of		
		1952	1953	1954	1955	Bayer 21/199	Diazinon	Parathion
Laboratory Strains 9,17	1949-50	0	0	0	0	(0.02-0.06)	(0.03-0.04)	(0.015-0.023)
Field Strain J-74	1955	?	P*s	Ps	Ps	1.7	.11	.06
" J-79	1955	?	Ps	Ps	Pg	(5-11)	.13	.09
" Z-98	1955	0	0	D**	B*** †	.9	—	.03
" Z 127	1955	0	Pg	D	B †	.9	.17	.05
" Z 129	1955	0	Pg	D	B †	.5	.09	.05
" Z 149	1955	P	Pg	D	D †	.6	.3	.06
" Z 150	1955	0	Pg	D	D †	1.3	.5	—
" F 151	1955	0	0	D	D †	.06	.13	.04

*P = parathion; **D = Diazinon; ***B = Bayer 21/199; Ps = parathion as an emulsion spray; Pg = parathion used as an impregnant on gauze strips; †= reported to be failing in effectiveness. Zero = exposure.

FIELD EXPERIENCES IN THE ECONOMIC CONTROL OF INSECTS WITH PARATHION

(1) Vs. Sitophilus granarius in wheat: Dusts at a dosage of 1% of grain w/w (0.25 ppm) protected grain 5 months; 1.25 ppm 12 months; 2.5 ppm gave 100% kills of S. granarius 37 months after grain dusting (100% mortality in 24 hr. exposures to grain 1 month after treatment.) 776
(2) Vs. Grasshoppers: More toxic than chlordane; 2% dusts at 10 lbs/acre gave fast kill (contact, 3267
fumigant). 1100
(3) Vs. Cicada septemdecom: Ineffective. 676,3368
(4) Vs. Aphrophora spp: More effective than DDT. 3327
(5) Vs. Psylla pyricola: Superior to HETP; 0.02% gave 100% kill (field) 0.001% gave 100% kill nymphs, 2705
0.045% gave 100% kill eggs (greenhouse). 2368
(6) Vs. Trialeurodes vaporariorum: 0.015% sprays yielded complete control. 353
(7) Vs. Rhopalosiphum rufomaculatum: 0.001% sprays yielded complete control. 2705,2870
(8) Vs. All greenhouse Aphids: Aerosols at 1 mg (parathion)/ft³ gave complete kills. 353
(9) Vs. Toxoptera graminum: 0.25 lb/acre gave ca. complete control. 353
(10) Vs. Pseudococcus comstocki: 0.025% suspensions gave good control. 353
(11) Vs. Pseudococcus maritimus: 0.03% suspensions gave complete control. 2358
(12) Vs. Pseudococcus spp: Considered the insecticide of choice; 10 g/hectoliter gave 100% kill; dusts at 0.5% = in effectiveness but slower and less regular; superior to HETP, TEPP, Nicotine, Rotenone, DDT, BHC, Chlordane, Aldrin, Dieldrin, Toxaphene® (many of which are ineffective vs. one or more stages) OMPA, BFPO, Systox®. 755
(13) Pseudococcus maritimus, P. citri, P. adonidum, P. gahani: Eliminated by 0.015% sprays. 2550
(14) Vs. Icerya: 0.03% sprays were effective. 57
(15) Vs. scale insects such as purple, citricola, yellow, California red, collon-cushiony, black scale: Effective control given. 475
(16) Vs. Coccus hesperidum and Saissetia hemisphaerica: Survived 0.025% suspensions. 2550
(17) Vs. Diaspis, Pinnaspis, Parlatoria, Chrysomphalus (scale insects): 0.015% sprays controlled. 2550
(18) Vs. Parlatoria oleae: Superior to HCN; especially toxic to eggs and young stages. 2947
(19) Vs. Thrips: Aerosols at 10 mg/ft³ controlled most types. 2870
(20) Vs. Heliothrips haemorrhoidalis and H. simplex: 0.015% sprays gave complete control. 2550
(21) Vs. Anticarsia gemmatilis: Superior to cryolite. 110
(22) Vs. Argyrotaenia citrana: Inferior to DDT. 2704
(23) Vs. Argyrotaenia velutinana: 0.025% - 0.006% suspensions yielded control. 1199,1235
(24) Vs. Polychrosis viteana: Only insecticide which kills insect within the grape. 3052
(25) Vs. Spilonota ocellaria: Gave economic control. 578,2073
(26) Vs. Pyrausta nubilalis: At 0.5 lb/gal as direct spray yielded 65% reduction, + 18% reduction by residual action. 675
(27) Vs. Melittia satyriniformis: Ineffective as a soil treatment. 1614
(28) Vs. Aegeria exitiosa: 0.025% sprays proved excellent; superior to DDT. 274
(29) Vs. Aegeria exitiosa (eggs): Single spray was residually effective for more than 13 days; exposures of 2-6 days were required for egg kill on sprayed surfaces; developed to hatching but larva failed to emerge from chorion. 2865
(30) Vs. Thyridopteryx ephemeraeformis: 0.1% sprays gave complete control. 2519
(31) Vs. Rhagoletis spp. 0.04% gave complete control. 625
(32) Vs. Aleurocanthus woglumi: Toxic to all stages as dusts and wettable powders. 2517
(33) Vs. Liriomyza flaveola: Controlled. 1691
(34) Vs. Epilachna varivestis: One of the most effective organic toxicants. 1619
(35) Vs. Popillia japonica: At 4 lbs/acre yielded 99% kill of larvae in 5 weeks; surpassed only by aldrin. 2776
(36) Vs. Cotinus nitida: 0.0002 lb/acre in soil yielded 90% control; superior to aldrin, dieldrin, lindane, chlordane, Toxaphene®. 822

(37) Vs. Diabrotica duodecempunctata: 1 lb/acre proved effective; surpassed by lindane. 1876

(38) Vs. Tychius griseus and Sitona hispidula: 1% dust at 45 lb/acre gave control on alfalfa. 1314

(39) Vs. Brachyrhinus ligustici: Dusts of parathion proved superior to sodium fluosilicate. 1312

(40) Vs. Conotrachelus nenuphar: 5 sprayings at 0.05% gave complete control (with some phytotoxic hazard). 778, 848,517

(41) Vs. Paratetranychus pilosus and Tetranychus bimaculatus: Greenhouse use at 0.004% yielded control. 2705

(42) Vs. Paratetranychus pilosus, Tetranychus pacificus, T. bimaculatus, Bryobia praetiosa, Vasates cornutus: Yielded outstanding control. T. pacificus, T. bimaculatus etc., are controlled by 2-3 applications of 15% wettable powder suspensions at 0.5 lb/100 gal. Against Septanychus parathion is reported no more effective than sulfur. Tarsonemus pallidus may be controlled by single sprays at 0.015%. Against Paratetranychus citri eggs 0.025% sprays were not effective. Reported ineffective vs. Brevipalpus and Tenuipalpus these being almost the only greenhouse arthropods not controlled by parathion aerosols at 1 mg/ft^3. 353

(43) Vs. Dermanyssus gallinae: Controlled by parathion treatment of poultry houses. 83

(44) Vs. Amblyomma americanum: Used as an area spray at 0.5 lb/acre pasture was disinfested for 2 months. 2167

(45) Vs. Wasmannia auropunctata: Complete control obtained with 0.05% sprays. 2423

(46) Vs. Aëdes spp: Complete kills at 1 ppm; almost complete control at 0.05 lb/acre (DDT at same dosage gave 57% control). 353, 1185

(47) Vs. Simulium damnosum: As a larvicide said to be less effective than DDT. 1549

(48) Vs. Myzus persicae on tobacco: 1% dusts yielded complete kills of aphids in 24 hours. 639

(49) Vs. Metatetranychus ulmi (England): 2 applications at 0.01% gave commercial control at least until August; at 0.06% yielded 100% elimination followed by several weeks control although reinfestations in August were heavier than elsewhere, including control orchards. High September "populations" common after applications at commercial strengths in June. 1807

(50) Vs. Musca domestica: (Laboratory tests as sugar, molasses baits) parathion at 1% yielded 13% down or dead in 30 minutes and 1 hour; 90% in 24 hours. 1915

(51) Vs. Carpocapsa pomonella (3 year field experiences 1950-1953): Considered one of the most promising toxicants; best control in orchards reported to be with parathion + DDT combinations. Tested with DDT, EPN®, Diazinon, Metacide CS 708, methoxychlor, Ryania (all of which were highly promising) among others, Parathion (and Metacide) were especially effective vs. eggs, young larvae in fruit and adults but were subject to a too rapid weathering. 1358

(52) For Parathion in tropical agriculture (Katanga, Congo Belge) see Ref. 1135.

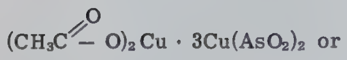
For screening test data consult: Ref. 1801.

ADDENDUM; CERTAIN MOST RECENT DATA ON PARATHION:

1) Relationship of ovicidal action of parathion to choline esterase in the eggs of Sanninoidea exitiosa and Oncopeltus fasciatus. N. B. Oncopeltus fasciatus eggs are not susceptible to the ovicidal action of parathion at practical concentrations. 2866
   - a) In eggs of Sanninoidea and Oncopeltus (incubation periods 8.5 and 6.1 days respectively at 80°F) choline esterase activity is manifest on ca. the 4th day thereafter increasing until hatching.
   - b) Ca. 3 times as much ChE activity is manifested by eggs of Sanninoidea (in advanced embryonic development) as is shown by eggs of Oncopeltus at equivalent stages.
   - c) Parathion yields choline esterase inhibition in eggs of Sanninoidea regardless whether treatment is applied before or after the embryogenetic appearance of the enzyme. This is interpreted to imply significant retention of toxicant by treated eggs.
   - d) The choline esterase for each species shows specific properties by which each differs from the other.
   - e) In vivo ChE inhibition by parathion is correlated with ovicidal effectiveness.
   - f) In vitro ChE inhibition, to the extent of more than 50% inhibition, is yielded by parathion for both the eggs of Sanninoidea and Oncopeltus, the former a susceptible and the latter a relatively non-susceptible species.
   - g) The following postulate of action is offered: Parathion is taken up at any stage to remain in the egg ready to inhibit ChE when this makes its embryogenetic appearance. ChE inhibition does not prove lethal until late in embryogenesis.

139

PARIS GREEN (Copper acetoarsenite; Schweinfurth-, Imperial-, French-, Vienna-, Parrot green; etc.)



$(CH_3C(=O)-O)_2Cu \cdot 3Cu(AsO_2)_2$ or

$3Cu(AsO_2)_2 \cdot Cu(C_2H_3O_2)_2$ or

$(CuOAs_2O_3)_3 \cdot Cu(C_2H_3O_2)_2$ Molecular weight 1013.7

GENERAL (Also consult the section titled, Arsenic, Arsenicals)

[Refs.: 484,2120,129,353,2815,1059,757,2226]

The most important of the copper and arsenic containing inorganic insecticides, having been in use since about 1867. For a long time, Paris green was the insecticide used most extensively against Colorado potato beetle. Although more modern toxicants are supplanting Paris green, ca. four million pounds are still in use on American farms, orchards and gardens each year. Paris green is above all a stomach poison high in arsenical toxicity with all the intense activity against all living organisms which this implies. Paris green is of intense toxicity for man and thus, under appropriate circumstances, has a high potential hazard. It is, in addition, again under certain circumstances, greatly phytotoxic. The instability of Paris green in the presence of water and carbon dioxide to yield phytotoxic arsenic compounds tends to limit use, at the present time, to insect baits and mosquito larviciding.

PHYSICAL, CHEMICAL [Refs.: 144,353,2815,1059,757,730,967,1027,732,733,731,145,1575]

An emerald green powder; odorless; virtually insoluble in water; insoluble in alcohol; soluble in acids and ammonia; a complex, somewhat indefinite compound of copper meta-arsenite and copper acetate at a ratio of 3:1 usually, but varying to as low as 2:1; now standardized as a definite compound of copper arsenite and copper acetate at a 3:1 ratio with an As_2O_3 content of 57%; the usual standard requirements are for the presence of at least 55% arsenious oxide, 20% cupric oxide and 10% acetic acid; homologues with other fatty acids, such as formic, butyric, propionic, valeric and succinic are unknown, although certain analogues are prepared with higher fatty acids (oils) which are insoluble in water and more toxic to some insects for instance Tribolium confusum than Paris green or lead arsenate and have the virtue that they can be ground very fine; decomposes readily in water to yield soluble arsenious oxide.

a) Formulations: Poison baits for cutworms, grasshoppers, armyworms; dusts (with lime) for use on tobacco; water suspension sprays with or without lime.

TOXICOLOGICAL

1) Toxicity for higher animals:
   - a) Paris green contains arsenic in the trivalent form in which arsenical toxicity is at maximum. 851
   - b) Highly toxic to man when taken by mouth. In contact with open skin wounds or abrasions tends to aggravate 851
     and induce suppuration. 1221
   - c) Particle size of Paris green powders exercises an effect on toxicity. 851
   - d) Quantitative:*

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Frog	sc	MLD	10		288
Rat	or	LD_{50}	ca. 22		1951
Rat	or	MLD	300		288
Guinea Pig	or	LD	30	Death in 4-5 hours.	288

*The toxicity of Paris green is intimately associated with the content of arsenic trioxide (As_2O_3) and attention is drawn to the general section on Arsenic and Arsenicals and the treatment of Arsenic trioxide.

2) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:
   - a) The action of Paris green is almost solely due to the arsenic content. 851,1221
   - b) The soluble, absorbable, inorganic compounds of arsenic are general protoplasmic poisons which react with functional groups of proteins and thus with protein enzymes to impair cell function at an elemental level. 851,1221
   - c) The details of absorption, distribution, excretion, mode and mechanism of action, pathology, etc., are covered in the section titled Arsenic, Arsenicals.

3) Hazard to wild life:
   - a) Indubitably hazardous, depending on the method of application and use.

b) When dusted on water as a mosquito larvicide, in which action it is almost specific, effects of a deleterious nature have been reported for fish. 245
(1) Not, however, persistent; probably converted to arsines and lost by volatility.

c) In France, in regions of heavy use for potato beetle control, deaths of many wild birds feeding on insects poisoned by Paris green have been reported. 527

4) Phytotoxicity:

a) Breakdown in presence of moisture, humidity and CO_2 yields soluble arsenic trioxide (As_2O_3) with consequent high toxicity for arsenic sensitive and tender plants, orchard trees, etc. Because of a tendency to burn severely plant foliage (as well as because of other disadvantages) Paris green has been largely superseded by lead arsenate for application directly to plants. 145 1575

b) Killing of peach foliage by direct plasmolysis of leaf tissue has been reported. 1079

c) May be "safened" for use on most field crops and pome fruits by the addition of lime. 2557

d) Never to be used on peach, cherry or plum trees, or other "stone" fruits. 2557

e) Application to apple-tree branches is tolerated if the bark is whole and unwounded. 2301

f) Begins to injure vegetation when used at 900 lbs per acre. 2301

g) Toxicity of Paris green and other compounds applied to cotton seedlings as solutions in a nutrient medium: 894

Substance	% Seedlings Damaged Beyond Recovery At				
	1:100	1:1000	1:10,000	1:100,000	1:1,000,000
Copper acetoarsenite (Paris green)	100	100	100	38.47	9.1
Tricalcium arsenate	53.85	76.93	9.1	7.7	0
Lead arsenate	100	100	33.3	0	0
Arsenomethane As-1,2-sulfide	100	70	12	10	0
Chloroarsenomethane As-1,2-sulfide	100	100	100	0	0
DDT	0	0	0	0	0
Control	0	0	0	0	0

5) Toxicity for insects: (Also see section titled Arsenic, Arsenicals)

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Ascia (=Pieris) rapae (larva)	or	LD_{50}	0.04(.02-.06*)mg/g	*=Intermediate zone	1381
Alabama argillacea (5th instar)	or	LD_{50}	0.01(.01-.03)mg/g		1103
Alabama argillacea (")	or	LD_{50}	0.04(.03-.08)	Paris green 1 + calcium arsenate 9	1103
Alabama argillacea (")	or	LD_{50}	0.09(.05-.15)	Paris green + calcium arsenate 7.25:92.5	1103

b) Effect of particle size on feeding and mortality in Epilachna varivestis adults: 2176

Substance	Particle Size (micra)	Average Deposit ($\mu g/cm^2$)	Amount Eaten/g Insect		% Mortality (In 48 Hrs.)
			Leaf Area (cm^2)	Insecticide (μg)	
Paris green	22	110	4.5	449	43
Paris green	12	105	2.3	238	61
Paris green	1.1	105	.3	34	88
Talc	4	108	44.8	4841	19

c) Comparative effectiveness of Paris green homologues vs. Tribolium confusum in flour with 10% toxicant; exposure 24 hrs. at 27°C, rel. humidity 50%:

Material	% Mortality
Copper acetoarsenite (Paris green)	51
Copper stearoarsenite	88 (65-100)
Soybean oil green	84 (63-100)
Linseed oil green	83 (63-100)
Fish oil green	56 (29-76)
Copper oleoarsenite	27 (17-35)
Copper crotonoarsenite	98
Copper lauroarsenite	92
Peanut oil green	91
Copper monochloroacetoarsenite	64
Copper dichloroacetoarsenite	62

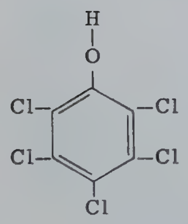
d) Effect on beneficial insects:
(1) Extremely harmful to foraging bees when applied as a spray to blossoming fruit trees. Like all arsenicals offers great hazard to bees. 3099
(2) Mortality of Hippodamia convergens with sprays at 1 lb/50 gallons applied by 5 methods for adults: Average kills: method I 85% (79-99%), II 34% (11-50%), III 93%, IV 99%, V 7%; average kill of eggs was 7% (0-15%) and of first instar larvae 3% (2-4%). 1450

e) Pharmacological, pharmacodynamic, physiological, etc.; insects:
  (1) For details see the section titled Arsenic, Arsenicals.
  (2) A purgative for Euxoa which in contrast to Pieris and Locusta retains a much smaller amount of the ingested toxicant (20% as against 35% and 40%) . 3206
  (3) Reported to repel Locusta migratoria migratorioides in poisoned baits. 3190
  (4) Causes relatively less damage to insect midgut epithelium (e.g. Prodenia, Vanessa, Locusta) than other arsenicals. 2510 3349

f) In economic control of insects:
  (1) Heliothrips haemorrhoidalis: Formerly controlled by baits and sprays of. 3400
  (2) Pieris rapae: 25% dusts control, but with phytotoxic and human hazard. 2226
  (3) Protoparce sexta, P. quinquemaculata: 15% dusts have controlled. 2226
  (4) Cirphis unipuncta, Laphygma frugiperda, Prodenia eridania have been combatted by 1% bran baits. 2226,349
  (5) Leptinotarsa decemlineata: Controlled by 0.4% suspensions with added lime. 353
  (6) Cylas formicarius: Effective against (as bait;) superseded by others. 561
  (7) Mosquito larvae: Still a first class mosquito larvicide as 1% dusts at 1 lb per 100^2 meters; 10 lbs per acre; however, DDT is superseding. 353

140

PENTACHLOROPHENOL (PCP; Penta; Penchlorol; Dowicide 7; Santophen 20, Santobrite)



Molecular weight 266.35

GENERAL [Refs.: 501,353,129,2120,2538,2221,1021,941,1538,1222,3136,1136,228,1801]

A compound which finds insecticidal use as a wood dressing to protect against termites and Lyctus beetles. Used also as a selective herbicide, and before-harvest leaf-drop inducer, as well as a general herbicide. Useful in the control of slime and algae, particularly in the form of the sodium salt (sodium pentachlorophenate). Both sodium and copper pentachlorophenates are active in very low concentration (10 ppm) in killing Australorbis glabratus, the mollusc (snail) vector of Schistosoma mansoni. Useful in the control of water hyacinth at concentrations innocuous to aquatic organisms but which retard growth of the hyacinth. The salts are water-soluble.

PHYSICAL, CHEMICAL

A colorless solid in the form of needle-like crystals; m.p. 190°-191°C; b.p. (with decomposition) 309°-310°C; $d_{4^\circ}^{22^\circ}$ 1.978; v.p. 0.12 mmHg at 100°C, 1 mmHg at 135°C; virtually insoluble in water 14 ppm at 20°C; freely soluble in alcohol, ether, benzene; solubility limited in cold petroleum ether, carbon tetrachloride, oils of low aromatic or olefine content; dissolves to 3% in fuel oil, to 32% in pine oil; volatile in steam; sublimes to needle-like crystals; non-flammable; odor is phenolic, pungent; non-corrosive to metals; deleterious to natural rubber when in oil solution; alkaline salts, for example sodium pentachlorophenate are water soluble, the sodium salt to 33 g/100 g water at 25°C; technical sodium pentachlorophenate is known as Santobrite; crude preparations are dark, greyish, in powder or flakes m.p. 187°-189°C.

a) Formulations: 5% in organic solvents, an example being Permasan 60.

TOXICOLOGICAL

1) Toxicity for higher animals: (General references: [1760,2062]).

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	sc	MLD	56		208
Rat	or	LD_{50}(ca.)	78		1951
Rat	or	LD_{50}	210	Single acute dose.	129,2120

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	125-200		2986
Rabbit	or	MLD	100		129
Rabbit	or	MLD	550		2170
Rabbit	or	LD	70-90	In fuel oil 5% solution; death in 2-5 hrs.	747
Rabbit	or	LD	130-160	In olive oil, 11% solution; death in 10-16 hrs.	747
Rabbit	or	LD	70-85	In olive oil, 5% solution; death in 3-6 hrs.	747
Rabbit	ct	LD	60-70	In fuel oil, 5% solution; death 1.5-4 hrs.	747
Rabbit	ct	LD	90-100	In furnace oil; 5% solution; death in 1.5-3 hrs.	747
Rabbit	ct	LD	40-50	In pine oil; 1.8% solution; death in 9-22 hrs.	747
Rabbit	ct	MLD	512.5		2170
Rabbit	sc	MLD	257		2170
Rabbit	ip	MLD	135.5		2170
Dog	sc	MLD	135		2170
Fish (19 species)	Medium	LC	0.2-0.6 ppm	Toxicity increased at pH <6.6	1222,941

2) Chronic toxicity, higher animals:
   a) No fatalities among rats, dogs receiving for 10-28 weeks in the diet 3.9-10 mg/day. 2120
   b) Dusts and vapors are very irritating to mucous membranes; induce violent sneezing. 2120
   c) The solid substance and solutions of more than 1% in strength are irritant to the skin. 2120
      (1) Contact dermatitis has been noted.
   d) In oil solution may be absorbed via the intact or unbroken skin. 129
   e) More toxic when dissolved in organic solvents. The dusts and vapors should be protected against and contact with eyes, skin and clothing avoided. 129
   f) MLD (as Santobrite) for 154 lb man estimated to be ca. 18 grams. 1538
   g) Rhesus monkey tolerated without effect 200 cc of water with 20 ppm Na pentachlorophenate. A calf drank 40 gallons of water with 20 ppm over a 4 day period without ill effect. Calves tolerated water with 60 ppm Na chlorophenate for 7 weeks, 51 ppm copper chlorophenate for 5 weeks and 46.5 ppm pentabromophenol for 6 weeks with no significant effects save slight enteritis. With molluscicidal use of these substances there seems to be a sufficient safety margin for stock. 1498

3) Symptoms of intoxication:
   a) Increased respiration and pulse rate; hypoglycaemia, diuresis, oliguria. 129

4) Hazard to wild life:
   a) Hazardous to fish which are killed by concentrations as low as 0.2 ppm. 1222,941,1021
      (1) In concentrations above 10 ppm fish appear to detect the presence of sodium pentachlorophenate. At concentration of 0.2 ppm 3 species of minnows survived. 3176
   b) Introduced into a flowing stream at 9.5 ppm destroyed the snail Australorbis glabratus completely for a distance of 1.5 miles downstream, but at this level was lethal to catfish, eels and guppies but not to crayfish. 228
   e) The lethal concentration for Daphnia magna (crustacean) = >5.0 ppm. 1021
   f) As Santobrite, lethal to 3 species of minnows at 0.4-5.0 ppm; longer survival at lower concentrations. 3176

5) Phytotoxicity:
   a) Highly phytotoxic, as evidenced by effective use as an herbicide, defoliant and growth retarding agent. 501,2120 129
      (1) At 15 ppm prevents algal growth in filtered water and halts algal growth in ponds in 7 days; 20 ppm halts algal growth at once, (as Santobrite). 1136
      (2) At 5 ppm Santobrite retards growth of water hyacinth, but 80 ppm is required for complete eradication; at the lower concentration most aquatic organisms are not harmed. 1538
      (3) Reported employment in the selective weeding of cereal crops. 501
   b) Kills plants only when direct contact is made with surface; no translocation. 129

6) Toxicity for insects:
   a) Structural modifications of pentachlorophenol alter toxicity as follows: 3265
      (1) With alkyl side chains added as ethers, insect toxicity rises with chain length from methyl to amyl, thereafter declining to a minimum at dodecyl pentachlorophenyl ether.
   b) Pentachlorophenol and hexachlorophenol constituted the halogenated phenols with most toxicity for insects, notably caterpillars and lice. 918,1801 2831,3033
      (1) In screening tests pentachlorophenol showed superior repellency for Aëdes aegypti.
   c) Superior to DDT in control of Lyctid beetles; Lyctus spp. eliminated by surface painting of wood with a 5% solution in fuel oil or naphtha. 1864
   d) Cerambycid beetles were controlled by surface painting of wood with 5% solutions. 353
   e) Vs. Scobius spp. reported as most effective (for a form toward which DDT was ineffective). 2648
   f) Vs. Termites: Reported to be the best all-round insecticide; in the case of Reticulitermes lindane and chlordane are more toxic and are used as additives for pentachlorophenol. 3354,3351 3241,1505
   g) Vs. Eutrombicula alfreddugesi and Acariscus mansoni (chiggers), used at 25 lbs per acre yielded complete control. 2024

h) Pentachlorophenol and chlorinated phenol derivatives vs. *Tetranychus telarius* on rose leaves as sprays (acetone, water, santomerse solution): 3265

Compound	Average Kill (%) Motile Stages At 1:500	Highest Dilution Yielding 90-100% Kill	Effectiveness Vs. Eggs, Resting Stages	Relative Phytotoxicity*
Pentachlorophenol	100	1:16,000	Excellent at 1:8000.	4
Alkyl ethers of " : Methyl	100	1:1000	Good at 1:1000.	0
Propyl	96	1:500	Excellent at 1:500	0
n-Butyl	94	1:1000	Good at 1:1000.	1
primary Amyl	97	1:1000	Good at 1:1000.	1
n-Hexyl	100	1:1000	Excellent at 1:1000.	2
n-Dodecyl	66		No control.	2
Allyl pentachlorophenyl ether	100	1:4000	Excellent at 1:4000.	4
Tetrahydro " "	100	1:1000	Excellent at 1:1000.	1
2,4-Dinitrophenyl " "	26		No control.	0
Benzyl pentachlorophenyl "	24		" .	0
2,4,6-Trichlorobenzylphenyl ether	68		" .	0
2,3,4,6-Tetrachlorophenyl-trichloro-benzyl ether	14		" .	0
2,4,6-Trichlorobenzyl 2,4,5-trichloro-phenyl ether	33		" .	0
Ethyl pentachlorophenoxyacetate	35		" .	0
2-Pentachlorophenoxyethyl acetate	100	1:2000	Excellent at 1:2000.	3
Butyl pentachlorophenoxyethyl acetate	100	1:4000	Excellent at 1:2000.	3
Ethyl tetrachlorophenoxyethyl acetate	100	1:2000	Excellent at 1:2000.	3
Butyl tetrachlorophenoxyethyl acetate	100	1:8000	Excellent at 1:2000.	4
1-Pentachlorophenoxy-2,3-propane diacetate	100	1:1000	Good at 1:1000.	3
Benzyl trichlorophenol	100	1:8000	Excellent at 1:4000.	4
Pentachlorophenoxy acetic acid	0		No control.	0
2-Pentachlorophenoxy ethanol	100	1:4000	Excellent at 1:4000.	3
2-(2',4'-Dichlorophenoxy)-ethanol	85		Poor at 1:500	3
1-(Pentachlorophenoxy)-2,3-propanediol	99	1:500	Poor at 1:500.	3
Acetone 65% control + H_2O 35% + Santomerse D at 1:3000	5.6		No control.	0

*4 = most phytotoxic, 0 = non-phytotoxic, between are other qualitative gradations.

i) Vs. *Anopheles quadrimaculatus* (larva, 4th instar) 10 ppm is the least concentration effective in yielding 100% kills; at 1 ppm 45% kill is reported. 2020

j) Vs. *Pediculus humanus corporis* 100% "knockdown" is yielded in 1 hour with 30-31 days of complete effectiveness in cloth impregnation tests. 2020

141

PETROLEUM OILS, MINERAL OILS, TAR OILS, ETC.

GENERAL [Refs.: 2117,353,2815,1059,757,523,2226,1523,3133,1594,630,1256,2114,2370,84,3197,3393,903, 3392,2696,2697,902,1179,1826,400,1177,759,2334]

Mineral oils in the crude state and in the form of refined or variously treated fractions have been long in use both for their intrinsic insecticidal powers and as solvents for other insect toxicants. They are particularly useful against the eggs of many insects and for such sap-feeders as aphids, scale insects and phytophagous acarines. They may be characterized, therefore, as direct insect killing agents or as "co-toxicants", solvents, carriers, stickers, stabilizers. The one essential, disadvantage of these agents is a phytotoxic hazard which must be minimized by various treatments. In general, two classes, for practical use, may be noted: Dormant oils and summer oils. Appropriate oil sprays are effectively used to control psyllids, plant bugs, mealy bugs, white flies citrus blackflies, thrips, aphids, buffalo tree hoppers, etc. They are effective ovicides for codling moth, oriental fruit moth, leaf-rollers, cankerworms and other lepidoptera. Toxicity to plants is associated with the presence of aromatics and unsaturated fractions. Their efficiency as insecticides increases with the paraffinic character of the oil. Viscosity is likewise an important factor. The light fractions, such as kerosene are solvents par excellence for many insecticides, for instance DDT. Mineral oils are incompatible with dinitrophenols and sulfur particularly on citrus plants but are compatible with cryolite and lime-sulfur. The phytotoxic hazard is lessened by use under cool and humid conditions and leaf-and fruit-drop have been recently minimized by admixture (to 4-8 ppm of the final, dilute spray mixture) of 2,4-D.

PHYSICAL, CHEMICAL, ETC.

1) According to origin, petroleum oil crudes are separable into 2 categories: 757
   a) Paraffinic oils, rich in saturated hydrocarbons (Pennsylvania oils).
   b) Asphaltic (naphthenic) oils containing aromatics, polymethylenes (naphthenes), sulfur compounds (mid-continent, Mexican, Gulf Coast oils).
      (1) Crude oils have been used (ca. 25% with water and emulsifiers) as dormant and summer oils; severely phytotoxic due to impurities.
      (2) Gasolines and naphthas (low boiling point fractions) are seldom used because of volatility, fire hazard, phytotoxicity, but are considerably toxic to insects such as green June beetles. 2798
      (3) Stoddard solvent (higher boiling naphtha, kerosene-like fractions) are used as solvents for insect control in furniture, mattresses, etc., where rapid evaporation is desirable. Used for spraying, flash points should not be <125°F. Typical specifications are: Initial b.p. 310°-370°F; 50% b.p. 340-380°F; final b.p. 390-412°F; flash point (tag open cup) 103°-140°F. 1547

2) Kerosene:
   a) Once used alone (or in emulsion with soap etc.) as an insecticide. 585
      (1) Low boiling point fractions less insecticidal than high boiling point fractions. 2298
      (2) Present main uses as: Carriers for household and cattle sprays of DDT, pyrethrins, and other contact insecticides.
      (3) Two classes: Light (b.p. 360°-480°F); heavy (b.p. 425°-510°F).
      (4) Properties vary, but in general are: Initial b.p. 360°-425°F, 50% b.p. 420°-440°F, final b.p. 480°-510°F, flash point tag 150°-185°F.
      (5) The kerosenes are hydrocarbons of 10-16 carbons per molecule and low viscosity.
      (6) Rapidly evaporating, they are useful in preparing residual sprays, of DDT for example, alone or with other solvents. Usually purified highly and made odorless for household sprays.
   b) Toxicity of kerosene:

Guinea pig	or	LD_{50}	ca. 20,380 mg/k	742
Rabbit	or	LD_{50}	ca. 28,350 mg/k	742
Rabbit	ip	LD_{50}	ca. 6,600 mg/k	742
Rabbit	iv	LD_{50}	ca. 180 mg/k	742

      (1) In man chronic intoxication has not been reported. 89
      (2) Signs and symptoms of intoxication, man: Following use of kerosene sprays in enclosed, badly ventilated spaces may occur: Head "fullness," blurred vision, dizziness, nausea, unsteady gait; massive exposure may bring collapse, nervous twitchings, coma, before the subject is warned enough to seek fresh air. Ingestion often brings instant gagging, coughing, aspiration into lungs. Profound drowsiness follows initial signs. Bronchopneumonia may ensue in 24-36 hours. Chest signs may be few or lacking, although Roentgen radiation shows extensive bronchopneumonia. Liver, kidney damage shown by liver enlargement and by albumen, cells and casts in urine. 89
      (3) Kerosene dermatitis is known and clears of itself when exposure ends. 89
      (4) For diagnostic aid (and with use of deodorized kerosenes the characteristic odor may be absent) consult Ref. 3315. 89

(5) Avoid oil laxatives, especially if kerosene was present as solvent for DDT or others; use sedatives and stimulants, if necessary, moderately. Chemotherapy does not aid kerosene pneumonia, but may, prevent bacterial invasion. Liver damage is minimized by a low fat and adequate protein diet. 89

c) Kerosene per se is toxic for insects, thus, in connection with other toxicants when it is used as vehicle it serves also as a toxic adjuvant. 757

3) “Light,” “Medium” oils: 757

a) Characterized as having higher viscosity, less volatility than kerosene.

b) For summer spraying light oils are used; viscosity 40-65 seconds, Saybolt; highly refined, mainly saturated hydrocarbons 14-18 carbons per molecule.

c) Medium oils are also used for summer sprays; viscosity 65-85 seconds, Saybolt.

d) Both light and heavy oils are employed alone or as emulsions.

(1) Paraffinic oils are more toxic for insects than corresponding aromatics (naphthenics).

(2) Low molecular weight fractions are low in insecticidal power; paraffinics of b.p. <670°F, viscosity <55 seconds, Saybolt are virtually non-toxic to eggs of Grapholitha molesta. For naphthenics a b.p. of 690°F and viscosity 110 seconds Saybolt are essential before marked insect toxicity is apparent.

(3) The “ideal summer oil” has been characterized as follows: Viscosity 80 seconds Saybolt at 100°F, n_D 1.464, $d_{4°}^{20°}$ 0.84, b.p. at 1 mmHg, 10°F, 50% b.p. at 760 mmHg 370°F, molecular weight 340. 524

4) Heavy oils, lubricating oils: [Refs.: 1745,881,1435,315,316,757]

a) Characterized by a Saybolt viscosity of more than 85 seconds. The lighter “lube” oils range in Saybolt viscosity from 70-110 seconds to 330-360 seconds.

(1) Used as dormant sprays. Not so highly refined as light and medium oils since, on dormant plants, phytotoxic hazard is less pressing.

(2) “Lube” oils are, in some cases, used as emulsions. Often combined with 2,4-dinitro-6-cyclohexylphenol, q.v., for added toxicity and smaller oil deposit.

5) Medicinal mineral oils such as Nujol®:

a) Highly refined white oils of Saybolt viscosity 150-250 seconds at 100°F (often employed as laxatives) have been applied to protect corn from Heliothis armigera. For this use the oil must be very pure. 178 757

6) Fuel oils: 757

a) These are heavier kerosenes employed as DDT solvents for biting fly control.

b) “Distillate” is used alone as a surface (water) spray vs. mosquito larvae.

c) Viscosity 34-40 seconds Saybolt, 50% distillation at 510°-550°F.

7) Gas oils: 757

a) b.p. 480°-570°F, 15-18 carbons per molecule; constitute the stove oils (b.p. 330-570°F) and the diesel oils (b.p. 400°-700°F) which because of high content of sulfonatable materials are too toxic for use on plants.

(1) May be refined as heavy summer oils.

8) Summer oils: 757

a) Fractions higher than kerosene employed in water emulsion on orchards and shade trees for control of mites and scale insects.

(1) The light summer oils (92% unsulfonatable residue) b.p. 52%-79% distilled at 636°F, Saybolt viscosity 40-65 seconds, 14-18 carbons/molecule.

(2) Medium summer oils: 28-49% distillation point at 636°F, Saybolt viscosity 65-85 seconds.

(3) Heavy summer oils: Viscosity greater than 85 seconds Saybolt, 10-25% distillation point at 636°F; must be refined to 94% or less unsulfonatable residue.

(4) Heavier oils may be used as dormant oils although some of these may be highly refined to 90% unsulfonated residue.

9) Naphthenes: 757

a) Volatile oils, too inflammable for insecticidal solvents. The highest fractions (flash point 140°F) may be employed on upholstery etc., as Stoddard solvents, b.p. 370°-412°F.

10) Methylnaphthalenes: 757

a) Components of asphaltic petroleums and coal tar oils.

b) Insecticidal per se; valuable DDT solvents (aerosols particularly).

(1) The highly refined fractions (Velsicols) are used in liquefied gas aerosols.

(2) Properties: d ranges from 0.922-0.993; viscosity, Saybolt at 100°F = ca. 35 seconds; minimum initial b.p. 415°-460°F; maximum final b.p. 520-680°F; flash point (open cup) 200-220°F; solvent power for DDT at 15°F = 25-35% w/v.

11) Miscible oils: 757

a) These constitute solutions of emulsifiers, such as cresylic and carbolic acid soaps, resinates, sulfonated fatty acids and petroleum-β-sulfonates in “gas” oils or “lube” oils.

(1) Readily emulsify on water dilution with stirring.

(2) Contain small amounts of water and a mutual solvent such as cresylic acid.

12) Pharmacology, physiological etc.; insects:

a) Killing of insects directly by mineral oils is looked upon (in the case of scale insects and eggs for example) as an asphyxiating effect of air exclusion. 757 523

(1) Kerosene sprayed on Musca domestica gives “knockdown” (narcosis by asphyxiation?) then progressive paralysis with recovery of locomotor activity from hind legs forward in 5-15 hours without injury. 2619

(2) In case of mosquito larvae kerosene and non-toxic oil films exercise an asphyxiant effect; larvae grow 2597
progressively lethargic and sink in 10-20 minutes the effect being anoxic. The same applies to *Sciara*, 382
Chironomus, *Drosophila*.

(3) Heavy oils on *Phenococcus* (scale insect) bring death in 5-15 days as does anoxia *per se*. 759

(4) Impurities in the oils add a true toxic action over and above anoxia; *Culex* larvae, for example, die from 2749
unrefined kerosene and fuel oil (even though in oxygenated water) with convulsions, twitches, and CNS 2597
histopathology (nuclear changes, chromatin clumping etc., in nerve cell body).

(5) Refined saturated oils may prove completely non-toxic, producing no symptoms of neurotoxic action or 2600
nerve destruction.

13) *Phytotoxicity:*

a) Oils may enter the plant directly through the leaf surface or via stomata. 3197,3392,757
1179,3133,902,3393

(1) Penetration of oil into leaf structure retards gas exchange, disturbs respiratory activity and 3392,2696,2697
reduces transpiration. 1826,757,400

(2) The physical presence of oil is not a factor since Nujol® does not kill foliage. 630,1177

b) *Toxic ingredients in oils:*

(1) Unsaturated olefins, aromatics, phenolic groups and sulfur compounds for example mercaptans. 759,523

(2) Benzene is highly phytotoxic; naphthenes are less toxic than benzene. Unsaturation enhances toxicity, 630
the unsaturated fractions being removable with SO_2, and H_2SO_4. Thus the term unsulfonatable residues refers to saturated compounds remaining after sulfonation to remove unsaturated substances and is *a measure of blandness toward plants*. The amount of sulfonatable material is a measure of the phytotoxicity of an oil.

(3) 5% kerosene emulsions with less than 16% sulfonatables are fairly safe on citrus (oil sensitive trees) 1256
at less than 25% sulfonatables moderately toxic, at more than 40% sulfonatables very toxic. On apple 3393
trees, oils with more than 15% sulfonatables are toxic to foliage; more than 45% sulfonatables are 630
toxic to buds. "Cracked" gasolenes (high in unsaturated components) are more toxic to cabbage than "straight run" gasolenes.

(4) Peach, plum and apricot trees are severely damaged by oils of 83% unsulfonatable residue composition; 2334
moderately damaged by 93% unsulfonatable residue oils; undamaged by highly refined oils. Petroleum 759
distillates of 50-60% unsulfonatable residue content cause leaf burn, leaf-drop and twig kill on orange trees; 98% unsulfonatable residue oils bring no injury.

(5) Highly refined oils show no acute phytotoxicity when properly used; the materials removed by refine- 630
ment are exceedingly phytotoxic. 3133

c) Damage to plants may be by acute toxicity (within 2 days) or by delayed toxicity which may take some weeks to manifest itself.

(1) Benzene, xylene and unrefined aliphatics (to C_{16}) such as kerosene, stove and fuel oils (and in hot 630
weather even heavier oils) yield acute toxicity with "burning," discoloration, leaf-drop, necrosis and 759
spotty foliage in apple trees. Such volatile oils do not develop delayed or "chronic" toxicity because 3392
of volatility and evaporation. Grasses and cereals are particularly susceptible to acute effects; carrots, 3393
celery, parsnips, parsley are highly resistant.

(2) *Chronic effects:*
Injury to young barley plants by petroleum oils: 630

Oil	% Injury On Stated Days After Foliage Wetting Sprays				
	1 day	2 days	4 days	7 days	9 days
White Gasoline	60	100	100	100	100
Stove Oil	75	100	100	100	100
Diesel Oil	30	75	95	100	100
Odorless Kerosene	0	10	25	100	100
Heavy Isoparaffin	0	0	5	20	40

a) Refined oils may show delayed toxic effects by secondary formation of toxicants such as asphaltogenic 3133
acids with -OH and -COOH groups. 0.5% of these in oil will injure peach tree foliage.

(1) Storage of an oil in light yields oxidative changes forming peroxides then acids in the presence of free 1594
oxygen; ultra-violet radiation is particularly active. Oils vary in time of onset of toxicity: In aromatics 630
immediate; in paraffinics after a latent period. Refined distillates, with natural antioxidants removed, are particularly susceptible to change.

(2) Such changes in an oil may take place at the plant surface or within it. 1594

(3) In the case of light, volatile evaporating oils "chronic" toxicity has no time to develop. The danger in- 1256
creases with decreasing volatility. Viscosity, determining the rate of leaf penetration, is a decisive 757
factor. For example, a high viscosity and low penetrability may compensate for elevated sulfonatable 2114
residue content. 2370

b) For safety summer oils must not be less than 90% unsulfonatable residue. In case of heavy oils of 94% 757
unsulfonatable residue, composition hazard increases with temperature, low humidity and very high 84,3197
humidity. 3393

(1) Penetration may be retarded by salts of oleic and stearic acids for instance, aluminum stearate is a 757
"safener" (on citrus) for kerosene and antioxidants. 1594,903

c) Mineral oils may injure fruit in growth, health, quality, flavor and appearance. The tree itself may be 3392,2370
irreversibly damaged by direct bark penetration with injury to the cambium. Translocation may take 757,2696
place from the foliage. Dormant oils may kill buds, twigs and tips. Bark blistering may develop. 1179,902

d) Plants differ in oil tolerance, for instance among citrus the scale of descending order in tolerance is: Lemon, grapefruit, Valencia orange, navel orange, tangerine, lime; tolerance is greater in cool or humid weather. 523

(1) Spindle oils $d^{15°}_{4°}$ .922 and .933; Viscosity at 20° 60 and 59; unsulfonatable residues 55 and 59; average molecular weight 260 and 276; $n^{20°}_{D}$ 1.5138 and 1.5206 were both highly phytotoxic to cucumber; in these two oils carbon chain content was 44% and 45%; saturated rings 34% and 36%; aromatic rings 20% and 21%. Furfural extracts were highly phytotoxic and the raffinate after 3 furfural extractions was still slightly phytotoxic. Sulfuric acid treatment removed all phytotoxicity. Unsulfonatable residues were increased by furfural to 73-76%, by H_2SO_4 to 96%-97%. At ca. 80% sulfonatable residues oils were toxic to cucumbers; at over 82% sulfonatable residues, such oils were safe. 1523

(2) Effects of a completely refined petroleum distillate on greenhouse plants; API gravity = 49-50, flash point = 170°F (open cup), boiling range = 370°-490°F, unsulfonatable residues = 98% or more viscosity = 30 seconds Saybolt at 100°F; highly volatile with high plant penetration. Applied by coarse sprayer, semi-coarse sprayer, fog sprayer: 0 = no injury, + = slight injury, ++++ = severe injury. 1189

Plant	Injury To Foliage		
	Coarse Sprayer (80% = ca. 175-200 micra* in diameter)	Semi-coarse Sprayer (80% = ca. 85 micra* in diameter)	Fog Sprayer (90% = 8-17* micra in diameter)
Begonia	+	+	0
Calceolaria	++++	+	0
Calendula	++++	+	0
Calla lily	—	—	0
Cineraria	++++	+	+
Carnation	++++	++++	0
Chrysanthemum	0	0	0
Cucumber	+	0	0
Boston Fern	0	0	0
Feverfew	+	0	0
Fuchsia	—	—	0
Heliotrope	—	+	0
Lantana	—	—	0
Lima bean	++++	+	+
Mulberry	+	0	0
Pelargonium	+	+	0
Primrose	++++	+	0
Rose	—	—	0
Smilax	0	0	0
Snapdragon	—	0	0
Stringbean	++++	+	0
Sweet pea	—	0	0

*Droplet diameter.

(3) Effects of a completely refined petroleum distillate applied to several insect species by fog sprayer; droplet size: 90% = 8-17 micra in diameter, 5% = 30-50 micra, 5% = 50-150 micra: 1189

Insect	Plants	Approximate Mortality (%) 48 Hours After Spraying
Aphids	Calla lily	100%
Mealy bugs	Pelargonium	100 (young; older plants 50%)
"	Mulberry	36
White flies	Carnation	100
Red spider	Rose	ca. 60
Scale	Palm	100
"	Lemon	100
Aphids	Calceolaria	90
"	Cineraria	100
"	Snapdragon	90
Red spider	Carnation	100
"	Smilax	100

Tests of the distillate specified above plus 0.5 lb. pyrethrum flowers (0.9% actual pyrethrins per gallon of distillate.) Fog spraying; laboratory tests:

Insect	Plant	% Mortality After 24 Hrs.	Plant Injury
Aphis rumicis	Nasturtium	100	0
" control	"	6.4	0
Thrips tabaci	"	100	0
" control	"	0	0

Insect	Plant	% Mortality After 24 Hrs.	Plant Injury
Heliothrips fasciatus	Bean	98	0
" control	"	0	0
Tetranychus telarius	Carnation	99	0
" control	"	8	0
"	Bean	99	0
" control	"	0	0
Pseudococcus comstocki	Tobacco	100	0
"	"	0	0
" control	Mulberry	92	0
←Field tests→		% Mortality after 48 hrs.	
Malacosoma americanum	Apple	100	0
Pseudococcus citri	Calla	90	0
Aleuroides vaporariorum	African daisy	95-100	0
Pseudococcus citri	Poinsetta	95-90	0
Macrosiphum sanborni	Chrysanthemum	100	0
Rhopalosiphum rufomaculata	"	100	0
Tetranychus telarius	Carnation	100(adults)	0
Chrysomphalus dictyospermi	Palm	90-100	0
Thrips tritici	Feverfew	70-80	0

14) Effects of petroleum oils on wildlife:

a) Harmful to aquatic life in 4 ways: Surface films emulsification, sedimentation + coating, toxic water soluble principles. 60

(1) Some oils, emulsified by agitation, are deadly to fish. 1309

(2) Crude oil, in concentrations down to 0.4 cc per liter (0.3 ppm ca.) proved very toxic to fresh water fish. 538

(3) Kerosene, as an insecticide at 25 gallons per acre, had no effect on fresh water fish. 1834

(4) Oil wastes act on epithelial and gill surfaces to induce asphyxia. 564

b) Tabulation of oil film thicknesses on water surfaces: 60

Gallons Oil/Mile^2 Of Surface	Film Thickness (in.)	Remarks
25	1.5×10^{-6}	Barely visible at best light conditions.
50	3.0×10^{-6}	Visible as silvery sheen on surface.
100	6.0×10^{-6}	First trace of color observable.
200	12.0×10^{-6}	Bright bands of color.
666	40.0×10^{-6}	Colors becoming dull.
1332	80.0×10^{-6}	Colors much darker.

15) Tar oils: (carbolineums, tar distillates, coal tar derivatives).

a) Highly phytotoxic products; applicable to plants only as dormant sprays. Effective primarily as ovicides (chiefly of aphids). 1059,757,2122 1436,1630

(1) Exceedingly variable in composition, depending on type, distillation, and the coking and illuminating gas by products so used.

(2) Differ from petroleum oils in predominance of aromatics over paraffinics and naphthenics. 2815

(3) Usual products of crude tar fractional distillation: 1059

To 210°C - light oils, benzenes, toluene, xylene.
To 210°-240°C - middle (carbolic) oils, phenols, naphthalene.
To 240°-270°C - heavy (creosote) oils.
To $>$270°C - anthracene oil, anthracene.

(4) Composition of representative coke-oven tars. (Complex mixtures of aromatic hydrocarbons with derivatives soluble in aqueous alkalis and tar bases soluble in dilute acids.) 3274

Fraction	% w/w Of Dry Tar
Crude benzene, toluene	0.3
Coumarone, indene etc.	0.6
Xylenes, cumenes and isomers	1.1
Naphthalene	10.9
Unidentified in naphthalene, methylnaphthalene range	1.7
α-Monomethyl naphthalene	1.0
β- "	1.5
Dimethylnaphthalenes	3.4
Acenaphthene	1.4
Unidentified in acenaphthene range	1.0
Fluorene	1.6
Unidentified in fluorene range	1.2
Phenanthrene	4.0
Anthracene	1.1

(4) Composition of representative coke-oven tars. (Complex mixtures of aromatic hydrocarbons with derivatives soluble in aqueous alkalis and tar bases soluble in dilute acids.) 3274

Fractions	% w/w Of Dry Tar
Carbazole and like N containing bodies	2.3
Unidentified in anthracene range	5.4
Phenol	0.7
Cresols, xylenols, phenol homologues	1.5
Tar bases (pyridines, picolines, lutidines, acridine etc.	2.3
Yellow solids of pitch oils	0.6
Pitch greases	6.4
Resinous bodies	5.3
Pitch (m.p. 238°C)	44.7

b) The low temperature distillates of tar contain more acids, paraffins, and naphthalenes than the high temperature distillates, which being rich in aromatics, bases and olefines are the more insecticidally important. 3373

(1) The most ovicidal fraction is a liquid neutral substance b.p. 280°-360°C (which also is less phytotoxic). Tar acids are disadvantageous for ovicidal use. 3145

c) Of the coal tar constituents, acenaphthene, anthracene, dimethylnaphthalene, fluorene and phenanthrene are relatively non-toxic as stomach poisons for Carpocapsa pomonella larvae. 2831

d) Certain standards for tar oils: 1434

(1) Tar oils, derived from bituminous coal tar heated at high temperature in gas retorts, or as a byproduct of coke ovens in illuminating gas manufacture should:

Distill in the following limits:

At temp. to 410°F (210°C) not > 1%
At temp. to 445°F (235°C) " > 10%
At temp. to 671°F (355°C) " > 65%

contain no more than 3% water and no more than 10% tar acids with less than 5% to be preferred; should remain free from crystals on 3 hours standing at 5°C, with occasional stirring.

e) Phytotoxicity:

(1) Highly phytotoxic, with phenol, creosols, xylenols and higher hydroxy-compounds being the principal 1059
toxic factors; however, removal of these reduces insecticidal and ovicidal effectiveness. 2120

f) Toxicity for insects:

(1) Higher boiling fractions (280°-360°C) are more effective vs. aphid eggs than fractions of b.p. 190-280°C. 1059

(2) 1.8-2.4% neutral tar oil will kill eggs of Aphis pomi; 4-5% concentration needed for apple scale. 353

(3) To control Aphis pomi, apple scale, Paratetranychus pilosus: A combined dormant spray of 3% petroleum oil + 2.5% neutral tar oil is effective; high concentrations injure dormant trees with greater injury in severe winters. 353

(4) Have been used as barriers vs. Blissus leucopterus. 3372

(5) Creosote oil fractions have been used in livestock dips. 353

(6) Action on insects is both asphyxiant and specifically toxic. 353

(7) When used against Eriosoma lanigerum tar oils are as harmful to the aphid parasite Aphelinus mali as to the eggs of the pest itself. 2381

(8) Have been used to control Phylloxera vitifoliae, various coccids and vs. eggs of Operophtera brumata. 353,1104

g) Hazard to man:

(1) Skin irritants, with a burning and caustic action. 353

h) Hazard to wildlife:

(1) Tar oils (tar acids) present at 0.1-0.3 ppm in estuarial waters have killed fish. 1714

(2) Commercial tar products (especially less viscous types) contain large amounts of water soluble toxicants.

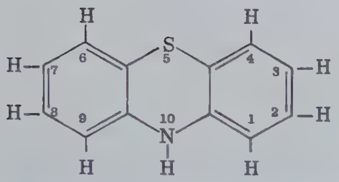
(3) Toxicity of effluents with 18.5 ppm tar acids (2.0 ppm tar basis) killed perch in 13 minutes. 1714

(4) Toxicity of "tar acids" for fish.

Sunfish	LC	70 ppm	Death in 1 hour.	2811
Sunfish	LC	66 ppm	"	1309
Sunfish	LC	13-33 ppm	" 1-3 days.	1309
Sunfish	LC	2.0 ppm	" 1 day.	1309
Trout (young)	LC	20.0 ppm	" 1 hour.	2142
Perch	Toxic Effect		As drainage from a tar road.	

142

PHENOTHIAZINE (Dibenzo-1, 4-thiazine; Thiodiphenylamine; Dibenzothiazine; Phenthiazine; Phenoxur.)



Molecular weight 199.26

GENERAL [Refs.: 458,2884,2885,2886,2622,314,76,3403,1215,353,2815,1059,757,2120,129,1801,1445]

A compound which first came to insecticidal notice as a mosquito larvicide and was later found to be effective against Carpocapsa pomonella (but with erratic and undependable action in large scale field tests under various conditions). Toward mosquito larvae reported to be more (or at least as) toxic than rotenone. Found to be toxic to tent caterpillars, Mexican bean beetle, grapeberry moth, European corn-borer, screw worm and other economic insects. Also possesses fungicidal properties. At the present time its greatest importance comes from use as an anthelmintic agent for the intestinal helminth parasites of domestic animals and livestock. Fully as effective (though erratic) as lead arsenate vs. codling moth. More than 3 million pounds were employed in 1951 to control nematode infestation in cattle, horses, sheep, goats, etc. Highly effective vs. Lucilia, Phormia, Cochliomyia, Culex, Chaoborus in the surrounding medium but mediocre as a contact poison for caterpillars, grasshoppers, roaches and beetles. None of the derivatives is as effective. Chiefly, phenothiazine (as insecticide) may be considered a stomach poison with a moderate selective action and with some contact activity.

PHYSICAL, CHEMICAL [Refs.: 2883,2120,2231,353,1215,739,1310,129]

A pale-yellow, crystalline solid (almost colorless when first sublimed) tasteless with a slight characteristic smell; darkens on exposure to light to a dark olive-green, probably through formation of polymers or isomers; m.p. 185.1°C; b.p. 371°C at 760 mmHg; sublimes at 130°C at 1 mmHg; virtually insoluble in water; freely soluble in benzene; soluble in ether, hot acetic acid; slightly soluble in alcohol and mineral oil; very slight solubility in petroleum ether and chloroform; readily oxidized in air and sunlight to phenothiazone and thionol; another oxidation product is phenothiazine sulfoxide which in air and light yields phenothiazone; phenothiazone and thionol act as oxidation-reduction systems with their leuco-forms; oxidation of films of phenothiazine in air may be largely prevented by such anti-oxidants as hydroquinone or a reductant such as mercaptobenzothiazole and also by Mischler's ketone, which inhibits absorption of ultraviolet radiation.

a) Formulations: As dispersible powders; in capsules and boluses mixed with salt and mineral mixes or feeds for antihelmintic purposes.

TOXICOLOGICAL

1) Toxicity for higher animals:

a) Not very hazardous as an acute toxicant a fact attested by its use as a vermifuge in veterinary medicine. 851
Use in man is unsatisfactory and photosensitive reactions may be anticipated at times in both animals and 1153
man following intake by mouth or contact with phenothiazine. 2524,2815

(1) Very effective in man against Enterobius vermicularis (pinworm, seatworm, etc.) but frequent sequelae of hemolytic anemia (and sometimes toxic hepatitis) contra-indicate such use.

b) Mammalian oral toxicity is relatively low. Oxidation products sensitize skin to light with consequent irritation followed by dermatitis. The total dose for man should not exceed 20 grams. For goldfish, phenothiazone is reported to be 10 times as toxic as phenothiazine. Dogs and cats survived 15 g doses although symptoms appeared at 3 g per animal.

c) Acute toxicity:

Animal	Route	Dose	Dosage (mg/k)	
Rat	or	LD_{50}	ca. 5000	1951
Rabbit	or	MLD	4000	2767
Cattle	or	MLD	500-1000	2265
Sheep	or	MLD	1000-2000	2265

d) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:

(1) Phenothiazine (and phenothiazone) do not in vitro inhibit Guinea pig liver catalase or beef heart cytochrome oxidase, although leucophenothiazone, leucothionol and thionol inhibit such systems actively. 569

(2) Phenothiazine showed an ID$_{50}$ for horse serum choline esterase at concentration of 6.7×10^{-5} M. 572,571

(3) The oxidation-reduction system, phenothiazone-leucophenothiazone, actively inhibits the oxidase and dehydrogenase factors of beef heart. 572,571

(4) The mode of toxic action has been suggested to be an irreversible oxidation of respiratory enzymes by the thionol-leucothionol system; anticholine esterase activity is also invoked as a factor. 571, 740

2) Phytotoxicity:

a) Reported to be low in phytotoxic hazard. A black spray residue may be disadvantageous in certain circumstances. 2120

3) Toxicity for insects:

a) As a stomach poison not effective against all insects, for instance: Non-toxic to Melanoplus bivittatus at dosages as high as 5.8 mg/g and without contact action toward Musca domestica. 2611, 353

b) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Ascia (= Pieris) rapae (larva)	or	LD$_{50}$	>1.12 mg/g		1381
Anopheles quadrimaculatus (4th instar)	Medium	MLC$_{100}$	1.0 ppm	5% kill only at 0.1 ppm.	2020
Bombyx mori (larva)	Contact Dust	LC$_{100}$	10%	In kaolin 90%; 100% kill after 3 days.	1190
Chaoborus astictopus (winter larva)	Medium	LC$_{100}$	0.33 ppm	Vs. over-wintering larvae.	768
Cochliomyia americana (larva)	Medium	MLC	0.03-0.05%	Concentration in culture medium.	2887 405

(1) Vs. larvae of culicine mosquitoes the LC$_{50}$ values for 6-methyl phenothiazine and 6-ethyl phenothiazine respectively are: 2 ppm and 5 ppm in 16 hours exposure to the phenothiazine containing medium. 1001

c) Comparative toxicity:

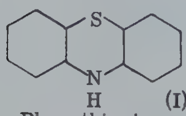
(1) Phenothiazine and other compounds vs. Chaoborus astictopus (overwintering larva): 768

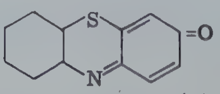
Insecticide	Concentration (ppm)	% Mortality
Penothiazine	0.33	100
Derris (as rotenone)	1.0	98.3
"	.5	97.5
L-Phenylbenzothiazole (in oil + CCl$_4$)	0.33	100
" "	0.2	99
" "	0.033	66
Pyrethrum (solution with wetting agent)	0.2	100
" "	0.1	93
" "	0.033	63
" "	0.016	36

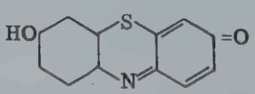
(2) Toxicity of Phenothiazine and related compounds for Cochliomyia americana (larva); toxicants in the culture medium: 405, 406

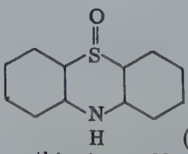
Compound	MLC (%) In Culture Medium
Acridine	0.01-0.03
Phenazine	.01- .03
Dibenzothiophene	.03- .05
5,10-Dihydroacridine	.03- .05
Diphenyl sulfoxide	.03- .05
**Phenothiazine	.03- .05
Phenothioxin	.03- .05
Diphenyl	.05- .08
Diphenylene oxide	.05- .08
9,10-Dihydroanthracene	.08- .10
Dibenzyl	.10- .17
Diphenylamine	.10- .17
Diphenylmethane	.17- .33
Phenoxazine	.17- .33
Phenyl ether	.17- .33
Phenyl sulfide	.17- .33
p-Dibenzodioxin	.33- .67
Anthracene	non-toxic
Carbazole	non-toxic
Diphenyl sulfone	non-toxic
Phenothiazine sulfoxide	non-toxic
Thianthrene	non-toxic

d) Structure and toxicity:


(I) Phenothiazine


(II) Phenothiazone


(III) Thionol


(IV) Phenothiazine sulfoxide

(1) The role of the oxidation products of phenothiazine in insect killing is unclear.
(2) Vs. Periplaneta americana: I, II = effective contact poisons; III is ineffective; I, II, III, IV are all ineffective as stomach poisons. 3403
(3) II is $\frac{1}{100}$-th as effective as I vs. Culex larvae. 1000
(4) II, IV are non-toxic for Carpocapsa pomonella and mosquito larvae. 1153
(5) II is fungicidal; I is non-fungicidal. 1215
(6) Vs. Epilachna varivestis only phenothioxin is comparable in toxicity to I; N-acetylphenothiazine, N-methylphenothiazine, tetranitrophenothiazine sulfoxide, dinitrophenothiazine sulfoxide all proved non-toxic. 1310
(7) I is a more effective stomach poison than N-methylphenothiazine, 3,9-di-methylphenothiazine, 3,5,7,9-tetramethylphenothiazine, N-ethylphenothiazine, N-acetyl-3,9-dimethylphenothiazine, N-acetyl-2,3,9,10-dibenzophenothiazine or N-acetyl-2,3,9,10-dibenzophenothiazone. 1969
(8) Phenothioxin is almost = to I vs. Culex larvae and is more effective vs. Phormia regina and Lucilia sericata; = in effectiveness vs. Cochliomyia macellaria. 1829
(9) The ether soluble fraction of commercial phenothiazine proved equal in effect when compared with the pure compound vs. Carpocapsa and mosquito larvae. 2883 2830

e) Data on the toxicity of various dibenz- compounds enclosing a heterocyclic ring with N, O, or S may be found in Refs. 2887,2128,1797,1182,3033,3034,406,1000,1381,410,2831,1595,2241.

f) Phenothiazine and beneficial insects:
(1) Virtually non-toxic to Apis mellifera. 231,927
(2) As a spray, at 2 lbs per 50 gallons by 3 application methods, phenothiazine yielded 100% kills of Hippodamia convergens adults; as a dust in talc gave 98% kills of adults and 100% kills of eggs and 1st instar larvae with spray applications; as a dust (1:10 in talc) gave 91% kills of 1st instar larvae. 1450

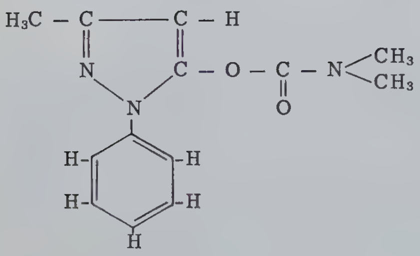
g) Pharmacological, pharmacodynamic, physiological, etc.; insects:
(1) Mode of entrance: Usually classed as a stomach poison. However, action on Epilachna varivestis is by contact and Periplaneta americana (with mouth parts sealed) is poisoned by dusting and hemolymph injection although no toxicity is reported via mouth by admixture with food or in suspensions. The impermeability of the intestine to phenothiazine is a suggested explanation. 1059 3403
(2) Pharmacological: Acts as a muscular depressant; no effect on the respiratory rate of the intoxicated insect.
  (a) Prodenia poisoned by mouth: Slow onset of depression and ultimate quiescence; no histologically detectable lesions. 3349
  (b) Periplaneta americana by topical poisoning: Locomotor ataxia passing to a flaccid paralysis; respiration rotenone-like; in the haemolymph a conjugate of leucothionol is believed the actual toxic principle. 3403
  (c) Chaoborus larva: The heart of poisoned Chaoborus may beat for 3 weeks and recovery occur after 4 days of immobility. 768
  (d) Blattella germanica: No effect on respiration (possibly a slight drop) even in the paralyzed insect poisoned by injection. 1441
(3) Physiological signs:
  (a) In Periplaneta: Failure of coordination in 5 hrs.; complete incoordination at 18 hours with the insect on its back. 3403
  (b) Popillia japonica (larva) may recover after lengthy paralysis caused by phenothiazine. 1310
(4) Biochemical:
  (a) In Periplaneta leucothionol appears in the haemolymph and symptoms begin when it reaches a threshold beyond which its effects can not be overcome by elimination. No phenothiazine (as such) appears in the haemolymph after contact poisoning. In oral poisoning phenothiazine is stored in the crop and converted to leucothionol in the midgut. 3403
  (b) Cytochrome oxidase (from Periplaneta coxal muscle in in vitro systems) is inhibited markedly at a concentration of 10^{-3} M as measured by O_2 uptake in Warburg's apparatus. Inhibition of respiratory enzymes has been postulated as the ultimate mechanism of action. 2305 3403
(5) Resistance:
  (a) A biotype of Cochliomyia americana resistant to phenothiazine has been selected out by 8 generations of breeding in a medium with 0.1% phenothiazine; only 3% of this biotype succumbed to 0.17% phenothiazine, a concentration at which 66% kill of non-R individuals was recorded. 1830

Field experiences in economic control of insects:
(1) Vs. Carpocapsa pomonella: High degree of protection. Less effective than DDT. 2115,1362
(2) Vs. Epilachna varivestis: Some effectiveness. 323
(3) Vs. Reticulitermes flavipes: Effective in control of. 1855
(4) Vs. Anopheles spp.: At 0.5-2 lbs per acre yielded good control. 2346,3146,3186
(5) Vs. Siphona spp.: Fed to cattle at 5 g/100 lb wgt: Larvae cannot develop in the dung of animals so treated. 2226

143

1-PHENYL-3-METHYLPYRAZOLYL-(5)-DIMETHYLCARBAMATE

(Pyrolan; Methylphenylpyrazolyl dimethylcarbamate; 3-Methyl-1-phenylpyrazolyl-(5)-dimethylcarbamate; G-22008 [Geigy].)



Molecular weight 246.282

GENERAL (Also consult Isolan, 1-isopropyl-3-methylpyrazolyl-(5)-dimethylcarbamate)

[Refs.: 1384,2231,1134,1119,1120,3273,1848,2659,2552,1317,1801,2120,851,1286,981,2942]

An insecticide of the general group commonly spoken of as carbamate or carbamic acid ester insecticides. (Consult, in this work, a general treatment of these insecticides titled, Carbamates, Carbamic acid Esters.) These insecticides have, in general, a powerful, inhibitory physostigmine-(eserine-) like action on choline esterase(s). Pyrolan is characterized by a swift pyrethrin-like action upon Musca, and a high contact toxicity toward aphids, thrips, bed bugs, granary weevils, etc. Effectiveness toward tetranychid acarines, such as Tetranychus bimaculatus, is low. Residual action of pyrolan is brief. Pyrolan reveals its full toxic activity on DDT-R biotypes of Musca domestica. Toward aphids, there are evidences of systemic poisoning action via the sap and juices of the treated plants. There is no good evidence of notable toxicity for lepidoptera. Introduced in 1950.

PHYSICAL, CHEMICAL [Refs.: 1132,1134,1119]

A colorless crystalline solid; m.p. 48°-49°C; volatile in steam; v.p. ca. 10^{-5} mmHg; soluble to 0.2% (2000 ppm) in water at 20°C; slightly soluble in petroleum oils; soluble in alcohol, acetone and aromatic hydrocarbons; soluble to 2% in kerosene; synthesis is via the enolization of 1-phenyl-3-methyl-5-pyrazole by heating with K_2CO_3 in benzene, then by reaction with dimethylcarbamyl chloride; odorless; tasteless.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	
Mouse	or	LD_{50}	62	1120,1119,1134
Mouse	or	LD_{50}	46	1384,2120
Rat	or	LD_{50}	90	1120,1119,1134
Rat	or	LD_{50}	53.5	1384
Rat	or	LD_{50}	62	2120
Dog	or	LD_{50}	75	1120,1134
Mouse	iv	LD_{50}	2.75	1120,1134

a) Reported to be more toxic than Dimetan, q.v., for mammals and less toxic than Parathion, q.v. 1317,981

2) Sub-acute and chronic toxicity:

a) Rats and mice receiving in the diet 10 mg/k/day showed no toxic effects. 1120

b) Rats and mice receiving in the diet 20 mg/k/day: After 1 month of exposure mice showed liver necrosis and fatty degeneration; rats showed no effects. 1120

3) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:

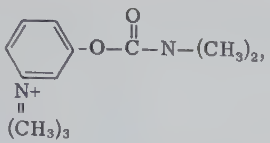
a) The ID_{50} concentration of pyrolan for the 50% inhibition of human plasma choline esterase = 6.1×10^{-7} M; for erythrocyte choline esterase the $ID_{50} = 1.2 \times 10^{-5}$ M. 2552

(1) A marked degree of specificity for the plasma esterase(s) is suggested. 2552

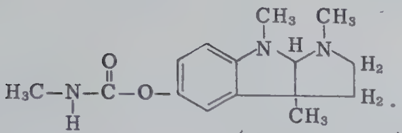
b) By inference it may be said that the effects of pyrolan on mammals stem primarily from the cholinergic effects and the intoxication consequent to them.

(1) Compounds with substituted carbamic acid groupings possess anticholinesterase activity and physo- 15,851

stigmine-(eserine-) like action; thus prostigmine, imitates the action of physostigmine 1452,2978 2961



(prostigmine)



(physostigmine)

The structural similarities of these two substances are apparent and their similarities to pyrolan (and isolan, dimetan and pyramat q.v.) are seen by comparison of formulae.

(2) As a choline esterase inhibitor pyrolan might be expected to affect those systems in which acetylcholine is a functional component, with far reaching consequences to the organism.

4) Phytotoxicity:

a) May injure plants at concentrations greater than 1%. 2120

5) Toxicity for insects: (Also consult certain data under Isolan)

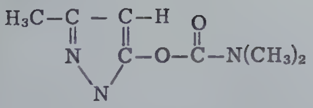
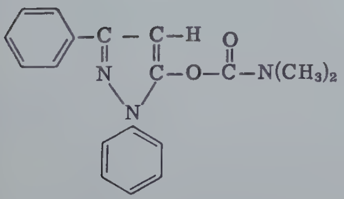
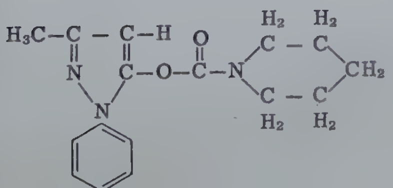
a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aphis rumicis (adult)	or	LD_{50}	0.0005 µg/insect, 0.8 µg/g	Action less rapid than Dimetan but final kill as great.	1119
Aphis rumicis (")	or	LD_{100}	0.001 µg/insect, 1.6 µg/g	" "	1119
Apis mellifera (adult)	or	LD_{50}	1.0-1.5 µg/insect, 13 µg/g		1119
Apis mellifera (")	or	LD_{100}	2.0 µg/insect, 18 µg/g		1119
Arctia caja (3rd, 4th instar)	or	Non Toxic	At 7-10 mg/g		1119,3273
Ceratitis capitata (adult)	Topical	LD_{50}	4.6 µg/g	ID_{50} (choline esterase inhibition) 2.8×10^{-8} M.	2659
Dacus cucurbitae (")	Topical	LD_{50}	1.2 µg/g	ID_{50} (") 7.8×10^{-8} M.	2659
Dacus dorsalis (adult)	Topical	LD_{50}	1.31 µg/g	ID_{50} (") 2×10^{-8} M.	2659
Ephestia kühniella	or	LD_{50}	0.005 µg/insect, 0.5 µg/g		1119
Ephestia kühniella	or	LD_{100}	0.0075 µg/insect, 0.7 µg/g		1119
Melolontha melolontha	or	Non toxic	At 50 mg/g	In olive oil solution.	1119,3273
Musca domestica (adult)	or	LD_{50}	0.05-0.07 µg/insect, 3.2 µg/g		1119
Musca domestica (")	or	LD_{100}	0.3-0.4 µg/insect, 27 µg/g		1119
Musca domestica (")	Contact Spray	Effective Dose	0.01 mg/cm^2		1317
Musca domestica (")	Contact Spray	LC_{50} 24 hr.	5.5 mg/cc	Turntable-Peet-Grady; KD 10 min at LC_{50}=100%.	2033
Periplaneta americana (nymph)	or	Non-toxic	At 10 mg/g	In olive oil solution.	1119,3273
Plusia gamma	or	LD_{50}	8 µg/insect, 24 µg/g		1119
Plusia gamma	or	LD_{100}	10-12 µg/insect, 30 µg/g		1119
Thaumetopoea processionaria	or	Non-toxic	At 7-10 mg/g		1119,3273
Vanessa io	or	Non-toxic	At 7-10 mg/g		1119,3273

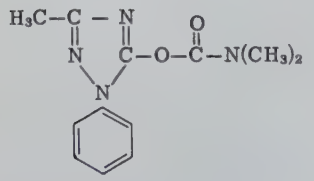
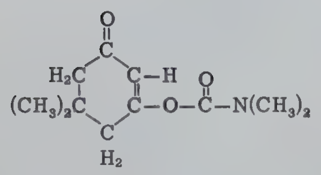
b) Comparative toxicity, pyrolan and other compounds for insects:

(1) More toxic vs. flies and other insects than dimetan, q.v.; some systemic action shown vs. Aphis pomi. Substitutions in the amine radical of the urethan group, additions to the phenyl group, substitutions for H in the 4 position of the pyrazolone nucleus and replacement of the methyl in position 3, all lead to losses of insecticidal activity more or less great. 981

(2) Vs. Dacus dorsalis, D. cucurbitae and Ceratitis capitata by topical application; LD_{50} and ID_{50} values (ID_{50} = concentration producing 50% inhibition of insect choline esterase(s): 2659

Substance	Vs. D. dorsalis		Vs. D. cucurbitae		Vs. C. capitata	
	LD_{50} (µg/g)	ID_{50}	LD_{50} (µg/g)	ID_{50}	LD_{50} (µg/g)	ID_{50}
Pyrolan	1.31	2×10^{-8} M	1.2	7.8×10^{-8} M	4.6	2.8×10^{-8} M
 G-22870	0.62	5×10^{-7} M	0.8	5.4×10^{-7} M	1.97	7.8×10^{-7} M
 G-23012	96.0	3.7×10^{-8} M	14.0	4×10^{-9} M	1.81	4.2×10^{-8} M
 G-23328	200.0	9.2×10^{-8} M	144.0	5.4×10^{-8} M	30.0	9×10^{-8} M

(2) Vs. *Dacus dorsalis*, *D. cucurbitae* and *Ceratitis capitata* by topical application; LD_{50} and ID_{50} values (ID_{50} = concentration producing 50% inhibition of insect choline esterase(s): 2659

Substance		Vs. *D. dorsalis*		Vs. *D. cucurbitae*		Vs. *C. capitata*	
		LD_{50} (µg/g)	ID_{50}	LD_{50} (µg/g)	ID_{50}	LD_{50} (µg/g)	ID_{50}
	G-23162	1720.0	9.2×10^{-6} M	288.0	8.2×10^{-6} M	96.0	8.4×10^{-6} M
	G-19258	117.0	5×10^{-7} M	128.0	6.5×10^{-7} M	92.0	5.6×10^{-7} M

(3) Pyrolan, dimetan and parathion vs. several insect species; oral administration; adult insects: 1119

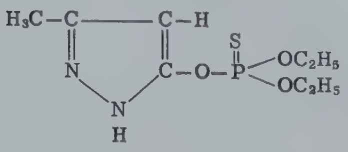
Insect	Pyrolan				Dimetan				Parathion	
	LD_{50}		LD_{100}		LD_{50}		LD_{100}		LD_{50}	
	µg/insect	µg/g	µg/insect	µg/g	µg/insect	µg/g	µg/insect	µg/g	µg/insect	µg/g
Plusia gamma	8	24	(10-12)	30	10	30	(12-18)	(36-54)	2.5	7.5
Apis mellifera	1-1.5	13	2	18	(1-1.5)	13	2	18	0.1	1.0
Musca domestica	(.05-.07)	3.2	(.3-.4)	27	(.05-.07)	3.2	(.3-.4)	27	0.01	0.5
Ephestia kühniella	.005	0.5	.0075	0.7	.005	0.5	(.01-.0075)	(.7-.75)	0.01	1.0
Aphis rumicis	.0005	0.8	.001	1.6	.0005	0.8	.001	1.6	0.0005	0.8

(4) Vs. *Musca domestica* (adult) as contact sprays, applied by a turntable modification of the Peet-Grady Method: 2033

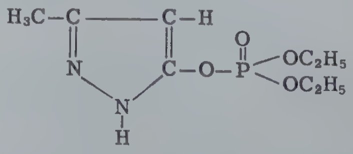
Insecticide	LC_{50} 24 Hrs. (mg/cc) (Conc. Required For 50% Kill In 24 Hrs.)	KD 10 Minutes At LC_{50} (%)
Pyrolan	5.5	100
Allethrin	1.5	100
Isolan	1.15	100
Dieldrin	0.017	0
Parathion	.02	0
Methyl parathion	.025	0
Lindane	.046	0
Heptachlor	.052	0
Aldrin	.056	0
TEPP	.069	ca. 70
Chlordane	.25	0
DDT	.35	0
Malathion	.48	0
Toxaphene®	.68	0
Tetraethyl dithiopyrophosphate	.69	0
Dilan®	.72	ca. 30

(5) Effect of structural modification on activity:

a) The potent insecticides Pyrazothion and Pyrazoxon q.v., are derived from the pyrazolone portion of pyrolan by the replacement of the dimethyl carbamate with the diethyl ester of phosphoric and of thiophosphoric acids. This change yields compounds which (in contrast to the carbamates) are active vs. lice and acarines: 1317



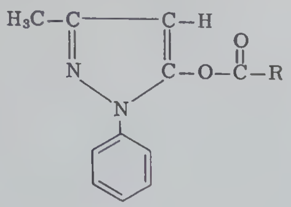
G-24027; Pyrazothion

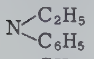
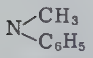
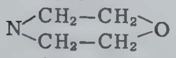
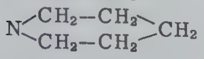


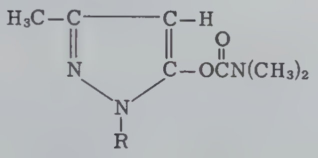
G-24483; Pyrazoxon.

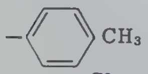
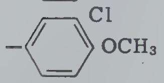
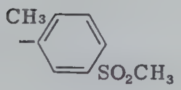
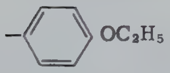
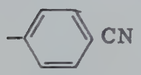
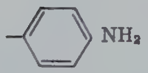
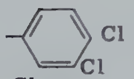
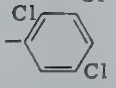
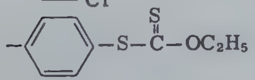
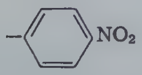
6) Activity vs. *Musca domestica* of substances of the type: 1317

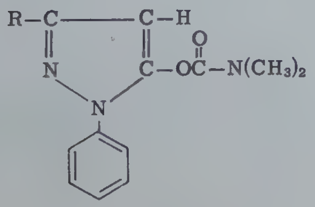
143. 1-PHENYL-3-METHYLPYRAZOLYL-(5)-DIMETHYLCARBAMATE



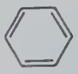
Designation	R	Effective Concentration As Deposits (mg/cm²)
Pyrolan	$N(CH_3)_2$	0.01
G-22007	$N(C_2H_5)_2$	10
G-23234	$N(C_3H_7)_2$	1
G-23323	$N(C_4H_9)_2$	10
G-23235	 $N{<}^{C_2H_5}_{C_6H_5}$	10
G-23236	 $N{<}^{CH_3}_{C_6H_5}$	>10
G-22873	 $N{<}^{CH_2-CH_2}_{CH_2-CH_2}{>}O$	No activity
G-23328	 $N{<}^{CH_2-CH_2}_{CH_2-CH_2}{>}CH_2$	0.1



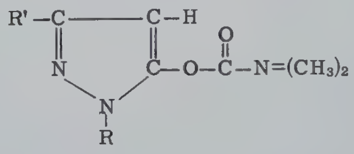
G-22417		10
G-22868		No activity
G-22869		"
G-22872		"
G-22955		"
G-22972		"
G-23007		"
G-23008		"
G-23015		"
G-23327		0.1

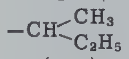
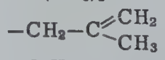
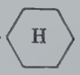


6) Activity vs. Musca domestica of substances of the type: 1317

Designation	R	Effective Concentration As Deposits (mg/cm^2)
G-23165	$-H$	0.1
G-23012	$-CH_2$ 	1.0
G-22418	$-COOC_2H_5$	>10

Modifications in the pyrazolyl portion of the molecule yield some products approaching parathion in toxicity for mammals and endowed with systemic action in plants (being transported in the sap stream like the systemic phosphoric acid esters) and having a wider spectrum of insecticidal action; among these derivatives is Isolan, q.v. As sprays, the action of these substances is of brief duration; to prolong the insecticidal action they must be applied by watering the soil, by treatment of tree trunks at the base, etc.



Designation	Activity As Deposits Vs. Musca (mg/cm^2) R' = CH_3	R	Activity As Deposits Vs. Musca (mg/cm^2) R' = H	Designation
G-22890	0.01	$-H$	0.01	G-23852
G-23612	0.01	$-CH_3$		
G-23224	0.01	$-C_2H_5$		
G-23629	<0.1	$-C_3H_7$	0.01	G-24001
Isolan	0.01	$-CH(CH_3)_2$	<0.1	G-23996
G-23842	0.01	$-CH_2CH = CH_2$	<1.0	G-24029
G-23613	0.01	$-C_4H_9$	1.0	G-24035
G-23884	0.01	$-CH_2CH(CH_3)_2$	1.0	G-23999
G-23890	<0.1	 $-CH{<}^{CH_3}_{C_2H_5}$	0.01	G-24000
G-24041	0.001	$-C(CH_3)_3$		
G-24080	0.01	 $-CH_2-C{\lessgtr}^{CH_2}_{CH_3}$		
G-23897	0.1	$-C_5H_{11}$		
G-23841	0.001	$-CH_2CH_2CH(CH_3)_2$	0.1	G-23997
G-24151	<1.0	$-C_8H_{17}$		
G-24344	<1	$-CH_2-$ 		
G-24152	<0.01	$-CH_2CH_2F$		
G-23883	0.001	$-CH_2CH_2OC_2H_5$		

7) Pharmacological, pharmacodynamic, physiological, etc.; insects: 1119,3273

a) Applied to thoracic ganglion of Periplaneta (=Blatta) americana: Tremors of the legs which were not reduced by decapitation before or after treatment.
   (1) Injection into head capsule, cerebral or oesophageal ganglia: Movements of mouthparts only.

b) The brain is not the site of action.

c) Action is central in ganglionic motor elements, not distal on the peripheral nerves. Applied as 0.1% solution in water to thoracic ganglion: Tremors of legs continuing after section of longitudinal elements and connections.
   (1) Severing of leg nerves close to ganglion: Immediate cessation of tremors.
   (2) Intact reflex arc essential for tremors; central action on motor region of ganglion.

d) Injection into prothoracic leg: Tremors in ca. 5 minutes followed by tremors in opposite leg in 8-10 minutes, in the mesothoracic legs in 40-50 minutes, in the metathoracic legs in 55-60 minutes.
   (1) Cutting of longitudinal connections brought cessation of hindleg tremors in 4-6 minutes; tremors in prothoracic legs persisted for 60 minutes.
   (2) Barbiturates, applied to ganglia, suppressed tremor; treatment of thoracic ganglion with nicotine suppressed tremor only in the legs of that segment.
   (3) Not transmitted by endoneural lymph canals; penetrates ganglia. Effect not reversed by washing.
   (4) Rapid decomposition in cockroach blood.

e) During tremor the respiratory rate rises; there is water loss; within 5 minutes CO_2 production was 4 times normal in Musca domestica. Blood acidity and muscle lactic acid increased in Periplaneta due to hyperactivity and clonic contraction of legs.

f) Death is by auto-intoxication, exhaustion and fundamentally due to cholinergic poisoning.

g) Pyrolan is ineffective vs. Psylla and almost ineffective vs. Paratetranychus.
   (1) Dimetan has a fast action on aphids, yielding 98% kills in 1 hour, with 90% kill in the 1st 20 minutes; Pyrolan acts more slowly, but with a final mortality as great as that caused by Dimetan.

144

PHOSPHORUS (Yellow phosphorus; Elemental phosphorus.)

GENERAL

Has been used as a paste to control cockroaches.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) The use of this material as an insecticide or rodenticide is to be deplored. To be effective it must be smeared on such materials as bread or other comestibles or be placed in baits which are dangerous to children and pets. Highly toxic to gallinaceous birds. 851

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rabbit	or	LD	7	Given in oil; death 2-4 days.	1540
Rabbit	or	LD	10	" " 3-4 days.	1054
Rabbit	sc	LD	12.5	" " in seven days.	2735
Rabbit	sc	LD	30	" " in seven hrs.	2735
Dog	sc	LD	2-3	" " 2-4 days.	2714
Dog	sc	LD ca.	12	" " 5 days.	3276
Rat	or	LD	$<$ 0.1 grain	Death in 8-24 hours.	2815

2) Toxicity for insects:

Insects	Route	Dose	Dosage	Remarks	
Blattella germanica	or	LD_{50}	$130 \mu g/g$	Also kills by contact.*	532
Periplaneta americana	or	LD_{50}	$20 \mu g/g$	Action slower than for NaF or Na arsenite	532

*When painted on the insect.

145

PHYTOTOXICITY (Some data for various trees and shrubs gathered by one investigator.)

1) Phytotoxicity of newer insecticides to ornamental trees and shrubs. 553
   a) Insecticides as mist concentrate formulations in Solvaspray 100 + commercial xylene. All treatments made in similar light conditions during July and August. Application to run-off (dripping) on both leaf surfaces made as an extreme application to evaluate the relative phytotoxicity of toxicants.
   b) Index: 0 = no injury, 1 = slight injury, 4 = moderate injury, 8 = severe injury, 10 = kill; (missing integers are gradations between the degrees of injury expressly defined).

Plant	Phytotoxicity Of 3% Solutions Of						
	Ovotran®	Aramite®	DMC	Chlorobenzilate	Compound 923	Xylene + Solvaspray	Average
Ulmus americana	1.4	1.3	9.0	7.5	—	0.0	3.8
Acer saccharum	6.3	8.7	9.0	9.3	—	1.1	6.7
Quercus borealis	1.0	1.5	8.3	0.9	0.6	0.0	2.1
Magnolia glauca	0.0	0.4	3.0	1.5	0.1	0.1	0.8
Viburnum lantana	4.5	8.0	9.3	1.5	3.9	0.3	5.4
Crataegus phaenopyrum	4.3	6.8	8.8	3.5	0.8	0.1	4.8
Malus sp.	2.9	8.3	9.0	0.9	8.5	0.0	5.9
Tilia cordata	6.0	8.5	9.0	7.5	8.0	0.0	7.8
Syringa sp.	4.0	9.5	10.0	1.0	6.9	0.0	6.3
Alnus glutinosa	2.3	3.5	8.0	8.3	2.3	0.1	4.9
Pinus strobus	0.1	0.0	0.4	0.3	0.0	0.0	0.2
Cercis canadensis	1.9	7.0	9.3	0.8	3.8	0.4	4.6
Salix sp.	6.0	8.0	9.0	7.0	3.0	0.0	6.6
Average	4.2	5.9	8.2	4.2	4.1	0.2	—

	Ovotran®	Aramite®	Malathion	Xylene-Solvaspray	Average
Oxydendrum arboreum	3.5	—	5.0	0.0	4.3
Cornus amomum	2.5	—	5.0	0.0	3.8
Deutzia scabra	9.5	—	7.5	0.8	8.5
Acer saccharum	6.3	8.7	5.8	1.1	6.9
Ligustrum obtusifolium	1.4	2.0	8.3	0.2	3.9
Lonicera sp.	8.8	9.8	9.0	0.3	9.2
Sorbaria sorbifolia	5.5	8.0	10.0	0.5	7.8
Eunonymus bungeanus	0.8	0.0	7.0	0.0	2.6
Aesculus parviflora	1.5	2.0	6.5	0.0	3.3
Viburnum dilatatum	8.0	—	6.5	0.8	7.3
Hydrangea sp.	2.0	5.0	8.0	0.0	5.0
Cotinus coggygria	6.0	—	7.5	0.0	6.8
Cladastris lutea	2.5	4.0	6.5	0.0	4.3
Syringa sp.	6.0	2.5	9.8	0.1	6.1
Average	4.2	5.9	7.1	0.2	—

Plant	Check Emulsion Xylene, Triton-X100, H_2O	Aramite®	Malathion	Ovotran®	Ovotran Formulations		
					C-1100	Proprietary	Average
Acer saccharum	5.7	8.0	—	8.0	5.8	10.0	8.0
Ligustrum obtusifolium	1.2	3.8	—	1.1	2.0	9.8	4.2
Syringa sp.	3.5	5.8	—	3.3	3.0	8.3	5.1
Hydrangea sp.	0.5	5.0	—	0.8	3.0	6.5	3.8
Lonicera sp.	3.5	5.8	—	4.8	4.0	9.0	5.9
Cornus amomum	2.0	—	9.5	5.0	2.5	10.0	6.8
Cotinus coggygria	3.0	—	4.5	5.0	5.0	9.5	6.0
Viburnum dilatatum	1.3	—	6.0	7.0	6.0	10.0	7.3
Cladastris lutea	8.0	7.5	—	9.5	6.5	10.0	8.4
Sorbaria sorbifolia	7.0	7.5	—	6.5	2.0	9.0	6.3
Eunonymus bungeanus	0.3	2.0	—	0.5	0.5	8.0	2.8
Aesculus parviflora	3.0	9.0	—	5.5	2.0	8.5	6.3
Average	2.9	6.0	5.9	4.8	3.9	8.9	—

Plant	Phytotoxicity Of 5% Solutions Of											
	Toxaphene®	Isodrin	Endrin	Aldrin	Dieldrin	DDT	Methoxychlor	Chlordane	Heptachlor	Lindane	Malathion	Average
Ulmus americana	1.9	1.4	1.9	1.9	1.2	0.4	2.4	5.5	7.5	8.4	8.8	3.7
Acer saccharum	4.8	0.0	3.3	1.1	1.8	2.6	0.0	2.5	2.5	4.5	3.0	2.4
Crataegus cordata	6.3	7.3	5.3	6.0	7.5	3.0	3.8	6.5	8.8	8.8	8.5	6.5
Pinus strobus	0.0	0.1	0.1	0.0	0.0	0.0	0.4	0.3	0.3	0.0	2.5	0.4
Populus sp.	6.3	1.3	6.8	1.5	1.5	4.3	4.3	5.8	6.5	7.3	7.0	4.8
Salix sp.	8.0	0.0	7.5	1.5	1.1	0.5	6.3	6.5	8.0	8.8	6.0	4.9
Quercus palustris	3.5	0.3	2.8	3.1	1.6	0.5	5.8	2.8	5.3	7.0	9.3	3.8
Carya ovata	1.4	0.3	0.8	0.3	0.4	0.5	0.8	3.8	3.3	8.0	10.0	2.7
Viburnum lantana	2.5	0.8	1.6	1.5	1.0	0.4	4.8	2.1	3.0	8.2	10.0	3.3
Average	3.7	1.2	3.3	1.8	1.6	1.4	3.5	4.5	5.1	7.3	7.7	—

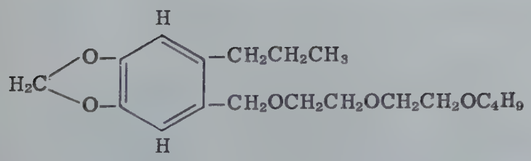
2) Safety limits within which certain insecticides may be applied to tobacco. (Place of test: Southern Rhodesia). 1716

Substance	Safety Limits; Doses in K Active Ingredient per Hectare		
	Germination (Seedbed)	Seedling (Seedbed)	Plant In Field
p,p'-DDT (80%)	112 (highest tested)	84.07 (highest tested)	3.36 (dust)
Parathion	8.4 (unburnt)	2.24	3.36 (dust)
"	2.47 (burnt)	—	4.48 (emulsion)
Toxaphene®	12.61 (unburnt)	—	4.21
"	7.17 (burnt)	—	
Chlordane	2.24	2.24	2.1 (dust) 11.99 (emulsion)
BHC (12% gamma)	0.2 (gamma)	no safety margin	0.3 (gamma) 1.12 (ploughed in)
BHC (25% ")	3.36 (")	"	0.93 (gamma)
BHC (95% ")	6.72 (")	2.02 (gamma)	1.05 (")

146

PIPERONYL BUTOXIDE

(α-[2-(2-n-Butoxyethoxy)-ethoxy]-4,5-methylenedioxy-2-propyltoluene; 6-(Propyl piperonyl)-butyl carbityl ether; 3, 4-Methylenedioxy-6-propylbenzyl butyldiethylene glycol ether; Butylcarbityl-6-(propylpiperonyl) ether.)



Molecular weight 338.43

GENERAL (Also consult piperonyl cyclonene).
[Refs.: 353,2231,1755,1597,314,2120,129,1221,3209,3165,3008,2344,249,833,324,1160,1508,3137,1444,3039,1801,1644]

A compound of mediocre insecticidal power, piperonyl butoxide acts as an effective synergist to increase the toxicity, persistence and "knockdown" effect of the pyrethrins and related insecticides such as allethrin. Essentially, piperonyl butoxide (like other insecticide synergists) potentiates the action of the pyrethrins, greatly elevating the toxic effect of a given quantity of pyrethrins so that a kill is produced greatly in excess of that which could be given by the pyrethrins alone under like circumstances. Piperonyl butoxide shows no synergistic or potentiating action with DDT, nicotine, sodium arsenite or sodium azide in some insects. There are reports of activation of rotenone, Ryania (ryanodine) and benzene hexachloride with piperonyl butoxide. Scabrin, also, is reported to be synergized by piperonyl butoxide. Synergism, however, with substances other than pyrethrins is of a minor order by comparison with the pyrethrin synergism given by this substance. Piperonyl butoxide is a derivative of piperic acid. The synergistic activity of piperine (an alkaloid from Piper nigrum) with pyrethrins against Musca domestica when observed led to the development of substances of more potent action of which the present compound is one. The activity of piperonyl butoxide (and related compounds) is thought by some to depend on the presence of the methylenedioxy-group in the molecular structure.

PHYSICAL, CHEMICAL [Refs.: 129,2120,3165]

A pale, yellow oily liquid, odorless and of faintly bitter taste; b.p. 180°C at 1 mmHg; $d_{4°}^{25°}$ 1.06; flash point 340°F; virtually insoluble in water; soluble to 100% in petroleum oil; soluble in dichlorofluoromethane, alcohol, benzol, Freon® and in most organic solvents; stable; non-corrosive; the commercial product consists of at least 80% of the compound whose formula appears above and not more than 20% related compounds which result from the process of synthesis, this being via the reaction of the chloromethyl derivative of dihydrosafrole with the sodium salt of the mono-n-butyl ether of diethylene glycol.

a) Formulations: Oil solutions, aerosols, dusts, wettable powders; used in combination with pyrethrins, ordinarily at 8:1 (5:1 to 20:1).

b) Analogues: Vs. Musca domestica the compound $CH_2O_2C_6H_2(C_3H_7)CH_2OCH_2CH_2OCH_3$ shows equal activity with pyrethrins at 10:1; several other analogues show a greatly lower activity and two compounds reveal "negative synergism," depressing the mortality of flies when applied with pyrethrins at 10:1. In these two last compounds the methylenedioxy-group is absent from the molecular structure. 3210

TOXICOLOGICAL

1) Toxicity for higher animals:

a) Used with safety (with pyrethrum or pyrethrins) on stored grains, cereal bags in homes and on animals where more hazardous materials cannot be used. Practically non-toxic and non-irritating to mammals or birds; non-carcinogenic; 42 ppm. in the total diet is considered a safe human tolerance concentration. 833,2120 129,2737 2738 3302

b) Acute toxicity:

Animal	Route	Dose	Dosage (mg/k)	
Mouse	or	LD_{50}	3.8 cc/k	806
Rat	or	LD_{50}	7.5-10.0 cc/k	2737
Rat	or	LD_{50}	ca. 11,500	1951
Rabbit	ct	LD_{50}	>1880	1952
Cat	or	LD_{50}	>10 cc/k	2737
Dog	or	LD_{50}	>7.5 cc/k	2737

c) Sub-acute and subchronic toxicity; chronic toxicity:

(1) Dermal absorption is poor. Multiple inunction at 200 mg/k may be fatal to animals. 129,1949

(2) Rats tolerated without harmful effects 5000 ppm in the diet for 17 weeks; 10,000 ppm were endured through 3 successive generations with moderate toxic effects. 129 1953

(3) 25,000 ppm in the diet were fatal to rats in from 4 to 46 weeks. 129

2) Phytotoxicity:

a) Apparently sufficiently safe from hazard to be compounded at 0.25% with pyrethrins 0.025%, rotenone 0.14%, rotenoids 0.25% in the Antrol® African violet and house plant aerosol bomb. 1061

3) Toxicity for insects:

a) Water miscible emulsions of piperonyl butoxide + pyrethrins (completely free of mineral oils or objectionable ingredients) may be applied directly to grain in storage to control insects. A standard concentration of 2% piperonyl butoxide + 0.2% pyrethrins (in oil free emulsion sprays) yields satisfactory and safe protection at 2-12 gallons emulsion per 1000 bushels grain. 833

b) Synergism of piperonyl butoxide with active principles of pyrethrum, and with allethrolone esters of chrysanthemum acids vs. Musca domestica by turntable test method: 1644

Substance	Alone		With Piperonyl Butoxide At 10:1 ratio		
	LC_{50} mg/100cc	Relative Effectiveness	LC_{50} mg/100cc	Relative Effectiveness (Rel toxicity)	Relative Synergistic Effect (column ~~5~~ / column ~~3~~) 4 / 2
Pyrethrins*	330	1.0	21.5	1.0	1.0
Pyrethrin I	190	1.74	21	1.02	.59
Cinerin I	420	.79	29	.74	.94
Pyrethrin II	490	.67	54	.4	.6
Cinerin II	740	.45	62	.35	.78
Pyrethrins*	350	1.0	17	1.0	1.0
Allethrin (dl-cistrans monoacid ester)	162	2.6	55	.31	.14
" (dl-trans monoacid ester)	135	2.59	60	.28	.11

Substance	Alone		With Piperonyl Butoxide At 10:1 ratio		
	LC_{50} mg/100cc	Relative Effectiveness	LC_{50} mg/100cc	Relative Effectiveness	Relative Synergistic Effect $\left(\frac{\text{column 5}}{\text{column 3}}\right)$ $\frac{4}{2}$
Allethrin (dl-cis monoacid ester)	325	1.08	105	.16	.15
" (d-trans monoacid ester)	85	4.12	30	.57	.14
" (dicarboxylic acid ester)	465	0.75	108	.16	.21

*Standard extract.

c) Piperonyl butoxide + pyrethrins vs. Sitophilus oryzae; mixed as dusts with wheat in 200 g samples at 0.357 g dust per 200 g wheat (100 lbs per 1000 bu) 78°-82°F; rel. humidity 48-50%; wheat moisture 11.8-12.98%: 3242

% Concentration Active Ingredients		Ratio	% Mortality At	
Piperonyl butoxide	Pyrethrins		7 Days	30 Days
0.80	0	—	10	11
1.2	0	—	11	21
0	0.2	—	49	79
0	.4	—	78	94
0	.8	—	95	99
0.25	.05	5:1	79	92
.4	.08	5:1	100	100
.6	.12	5:1	100	100
.4	.04	10:1	86	93
.6	.06	10:1	94	99
.8	.08	10:1	99	100
.5	.0375	13.3:1	88	96
.7	.0525	13.3:1	96	99
.6	.03	20:1	74	96
.8	.04	20:1	91	99
Control	—	—	10	17

d) Inhibits development of Musca domestica in CSMA* larval medium at 0.25-0.074% by weight; length of larval life is directly proportional to concentration and % adult emergence inversely proportional. Death occurred in the 3rd instar or in early pupation. Both normal and DDT-R strains were similarly affected, although in the DDT-R strain the effect was greater. Fly lipase added to the rearing medium does not overcome the piperonyl butoxide action. 2287

4) Pharmacological, pharmacodynamical, physiological, etc.

a) For succinct general treatments of synergistic action of insecticides and synergistic compounds (with theories of the mechanisms involved) consult Refs. 353,2231,3037,1597.

b) Tested for synergistic action with pyrethrins vs. mosquitoes in flight (as sprays) and Sitophilus granarius crawling on film deposits from oil solution, a sharp limitation of synergistic action was obtained when synergist pyrethrins were in equimolecular proportions in case of N-isobutyl undecyleneamide, ethylene glycol ether of pinene, piperonyl cyclonene, N-propyl isome and N-(2-ethylhexyl)-bicyclo [2,2,1]-5-heptene-2,3-dicarboximide but not in the case of piperonyl butoxide for which the limiting relative potency was not at equimolecular proportion. 249

(1) Tested with pyrethrins and allethrin vs. Musca domestica and Cimex lectularius by the measured drop test and topical application toxicity was observed to rise with rise in ratio of synergist to insecticide to at least 20:1; enhancement was greatest for lower ratios, falling off with increases. Piperonyl butoxide, the most powerful synergist, enhanced by 5 times the potency of pyrethrins and by 4 times the potency of allethrin toward flies. Piperonyl butoxide enhanced the toxicity of pyrethrins toward Cimex by 2 times and that of allethrin by 3 times. Piperonyl butoxide prolonged greatly the effectiveness of pyrethrin residual films. 2344

5) Control of economic insects:

a) Formulated with pyrethrins and impregnated in pulverized wheat as Pyrenone® Wheat Protectant (piperonyl butoxide 1.1%, pyrethrins 0.08%) the result is a mixture of minimum hazard to man and animals and with outstanding protectant value when applied to newly harvested wheat of high moisture content and held in storage in wooden bins. Recommended to be used at 75 lbs per 1000 bushels. The protectant was applied in the truck beds with mixing during the binning process. Protection was afforded vs. Cadelle beetle (Tenebrioides mauritanicus), grain beetles (Laemophloeus spp.) and the saw-toothed grain beetle. 3302

(1) Pyrenone with 4 ppm pyrethrins and 40 ppm piperonyl butoxide conferred complete protection (for at least six months) to wheat vs. Sitophilus granarius. 521

b) Vs. Periplaneta americana and Blattella germanica piperonyl butoxide 1% + pyrethrins 0.05% yielded immediate "flush" of the insects, rapid "knockdown" and fast and complete kill; no health hazard of any kind was involved. 824

---

*Chemical Specialties Manufacturers' Association.

c) Vs. Musca domestica piperonyl butoxide permits great reduction of pyrethrin content of insecticide formulations and can enhance residual pyrethrin toxicity to as long as 11 weeks; less effective, perhaps, than chlorinated hydrocarbons but without health hazard. 2151 971

d) Vs. Heliothis armigera with pyrethrins: Less effective than DDT. 158

6) Piperonyl butoxide in synergism with pyrethrins against various resistant biotypes of Musca domestica: 373

Strain (Resistant to Substance in Name)	Generations Of Insecticide Exposure	Strain Origin	LD$_{50}$ 24 Hrs., Topical For Piperonyl Butoxide + Pyrethrin 10:1 (μg/g)
DDT-I	21	Laboratory-I	88.7
DDT-W	3 yrs. in field	Field	74.8
DDT-III	4 yrs. "	Field	65.8
Methoxy-I	21	Laboratory-I	80.2
Lindane-I	21	Laboratory-I	62.5
Multi-I	8	DDT-I	89.9
Laboratory-I (non-R)	—	NAIDM	56.8
Laboratory-II (non-R)	—	Univ. of Indiana	49.1
Pyrethrin-I (Pyro-I)	21	Laboratory-I	258.7
Multi-III	8	Methoxy-I	81.6

7) Synergistic action of Piperonyl butoxide when applied at different intervals after previous pyrethrum treatment of Musca domestica: 272

a) PBO enhanced pyrethrum toxicity even when applied after the insecticide.

(1) With a high ratio of synergist to insecticide substantial kills were obtained with the synergist applied 8 hours after the insecticide.

(2) At similar concentrations, injection application of the synergist was more effective than topical application to Musca previously pyrethrum-treated.

Treatment	Interval Between Pyrethrin And Synergist Application (Hrs.)	Topical				Injection Of 1μg/fly PBO After 0.1μg/fly Topical Pyrethrin	
		0.1μg/fly Pyrethrin 10μg/fly PBO		0.1μg/fly Pyrethrin 1μg/fly PBO			
		% KD 30 min.	% Kill 24 hrs.	% KD 30 min.	% Kill 24 hrs.	% KD 30 Min.	% Kill 24 Hrs.
Pyrethrum + PBO	1	100	100	70	25	90	65
"	2	95	95	70	35	95	60
"	3	90	95	60	40	85	70
"	4	20	90	30	30	20	60
"	5	20	95	20	15	0	30
"	6	0	85	0	0	0	35
"	7	0	70	0	0	0	30
"	8	0	45	0	0	0	30
Pyrethrum (alone)	—	0	0	0	0	0	0
PBO (alone)	—	0	5	0	0	0	5

8) Addenda Recent data on the activity of Piperonyl butoxide:

a) Metabolic fate of C^{14} labelled piperonyl butoxide (α-[2-(2-n-butoxyethoxy)-ethoxy]-4,5-methylenedioxy-2-propyl-toluene-α-C^{14}) in Leucophaea maderae; analysis by paper chromatography. 2764

(1) After topical administration to ♂ and ♀ Leucophaea maderae the absorption and excretion of radioactive piperonyl butoxide was as follows: 88% of given dose absorbed in 3 days; ca. 50% of the applied radioactivity recovered from feces in 7 days; $<50\%$ of the recovered radioactivity attributable to unchanged PBO, the balance being as unidentified, water-soluble radioactive metabolites.

(2) Distribution of piperonyl butoxide in the tissues is as follows: In the ♀ radioactivity is distributed in brain, thoracic ganglia, foregut, hindgut and malpighian tubules, these tissues containing the greatest amount per unit weight. Little radioactivity in other tissues.

(3) The foregoing leads to the postulate that insect nerve tissue, foregut, hindgut and Malphigian tubules are involved in the metabolic degradation of piperonyl butoxide.

b) Effect of piperonyl butoxide on the anti-choline esterase action of certain organic phosphorus compounds for Musca domestica and bovine erythrocyte choline esterases: (Also consult malathion). 2576

(1) Piperonyl butoxide has depressed the toxic action of topical malathion on DDT-R and DDT-non R biotypes of Musca domestica while enhancing markedly the lethal action of diazinon and Bayer L 13/59 (Dipterex®).

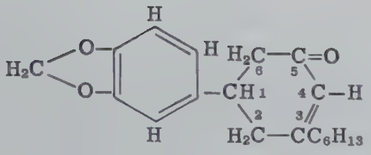
(2) In tests of the effect of PBO on anti-choline esterase activity, PBO depressed the anti-choline esterase action of malathion, the effect being more pronounced for purified, true acetocholine esterase than for Musca choline esterase in vitro.

(3) In vivo protective effects of PBO are shown in Musca when PBO is used as a pre-treatment prior to topical malathion. PBO applied 6 hours after topical malathion still revealed protection of choline esterase from the insecticide. No protective effect was shown with a 16 hour interval between PBO and malathion applications.

(4) PBO with diazinon and Dipterex® (Bayer L 13/59) yielded a synergistic toxic effect in topical application. No in vitro effect of PBO on the anti-choline esterase activities of diazinon or Dipterex® was noted.

147

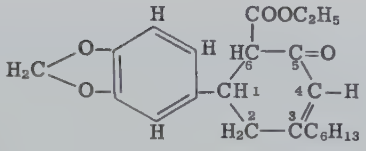
PIPERONYL CYCLONENE (3-n-Hexyl-5-(3, 4-methylenedioxyphenyl)-2-cyclohexenone, [I],+the 6-Carbethoxy-derivative of I[=II] 7: 3; Piperonyl cyclohexenone; 3-Hexyl-5-(3, 4-methylenedioxyphenyl)-2-cyclohexene-1-one; (3-Isoamyl-5-methylene dioxyphenyl)-2-cyclohexenone.)



[I]

(7 parts)

+



[II]

(3 parts)

GENERAL (Also consult piperonyl butoxide)

[Refs.: 353,2231,2120,129,1597,1801,249,77,1078,2476,1755,3011,314,1327,3164,1444,3039,3037,1476, 2590,3209,3039]

A substance which possesses, *per se*, modest insecticidal powers, but which is primarily a synergist for pyrethrins and such related insecticides as allethrin, whose toxic action is potentiated by the synergist, permitting a sharp reduction of their quantity in insecticidal formulations. Piperonyl cyclonene synergizes with DDT to lower the DDT resistance of DDT-R *Musca domestica*, but does not potentiate the action of DDT vs. normal, susceptible biotypes. Piperonyl cyclonene is a derivative of piperic acid and its development stems from observations made on the synergistic action of piperine (from *Piper nigrum*) with pyrethrins. As in the case of piperonyl butoxide and other synergistic substances the presence of the methylenedioxy-group is considered to have direct bearing on synergistic action. Piperonyl cyclonene is notable for low toxicity and hazard toward man and animals. Less effective than piperonyl butoxide. Said to synergise with *Ryania*, q.v.

PHYSICAL, CHEMICAL

The crude or technical product is a thick, reddish-brown, oily liquid; of the two components of the mixture, I* is a white, crystalline solid m.p. 59°C and II* is a light, viscous, oily liquid which is not distillable because it decomposes with heat; b.p. (tech. mixture) 180°C; d^{20° 1.09-1.20, d^{25° 1.136; virtually insoluble in water, petroleum oils and dichlorodifluoromethane; soluble in some organic solvents; odorless; stable; flashpoint 290°-300°F; non-corrosive.

a) Formulations: With pyrethrins in ratios of 8-12: 1 w/w chiefly in the form of dusts.

TOXICOLOGICAL

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage	Remarks	
Mouse	or	LD_{50}	5.1 cc/k		842
Rat	or	LD_{50}	6.9 cc/k		842
Rat	or	LD_{50}	ca. 5200 mg/k		1951
Rat	or	LD_{50}	7.5-10 cc/k	Undiluted.	77
Rabbit	or	LD_{50}	5-7.5 cc/k	" .	77
Cat	or	LD_{50}	>10 cc/k	" .	77
Dog	or	LD_{50}	>7.5 cc/k	" .	77
Rat	or	LD_{50}	>5 cc/k	Emulsion concentrate 4% + pyrethrins 0.2%.	77
Rat	or	LD_{50}	5-7.5 cc/k	50/50 Emulsion conc. + D and O solvent.	77
Rat	sc	LD_{50}	>10 cc/k	" " .	77
Rabbit	or	LD_{50}	>5 cc/k	" " .	77

---

*See formulae above.

a) At 0.3 cc (undiluted) at 0.1 cc in oil solution 5%, at 0.2 cc in water suspension 5%: Irritating to the eyes of rabbits. No irritation to skin of rabbit on repeated application undiluted, in oil and in water suspension. Multiple skin applications of 100 mg/k were supported well by rabbits. 77 1952

b) Animals (probably rats?) fed at a level of 5000 ppm in diet for 16 weeks remained in good health and gained weight. 129

2) Phytotoxicity:

a) Reported to be non-phytotoxic and, indeed, to stimulate plant growth. 129

b) Recommended for use with pyrethrins on garden pests and on flowering and ornamental plants. 129

3) Toxicity for insects:

a) Vs. Anopheles quadrimaculatus (4th instar): 762

Concentration	% Mortality After	
	24 Hrs.	48 Hrs.
10 ppm	60	100
1 "	10	90
0.1 "	5	50

b) Synergistic action with pyrethrins vs. Periplaneta americana ♀♀, exposed to dusts applied at 30 mg per area of 4.37 cm in diameter; laboratory tests; dust base = fullers' earth: 2513

Pyrethrins (%)	Piperonyl cyclonene (%)	% Mortality (10 days)
0.3	0	2
0	3	5
0.3	3	83
0.3	1.5	98
0.3	0.75	63
0.15	3	77
0.15	1.5	45
0.15	0.75	27

c) Action of piperonyl cyclonene on DDT-R Musca domestica: 2476,3318

(1) Applied topically to Bellflower strain of Musca (DDT-R), the LD_{50} was reduced from 7.4μg/fly to 1.1μg/fly; in the case of super-Laton (DDT-R) flies, LD_{50} was lowered from 2.5μg/fly to 0.2μg/fly, although susceptibility could not be restored to original levels. Susceptibility of DDT-non R biotypes could not be enhanced. Similar results, but less effective synergism, with methoxychlor-R and DDD-R Musca. The effect is considered to be due to retardation of the enzymic detoxification of DDT (dechlorination to DDE) in DDT-R biotypes. 2478

d) Action on Periplaneta americana exposed to C^{14} labelled DDT and DDE topically applied; adult ♀♀ at 28°C: 2675

(1) Radioactive DDT, applied topically, is rapidly absorbed, widely distributed internally and as much as 75% of the amount applied is excreted as metabolite(s) in the feces.

(2) Piperonyl cyclonene, used with DDT, inhibited DDT absorption and metabolite excretion.

4) Pharmacological, pharmacodynamic, physiological, etc.:

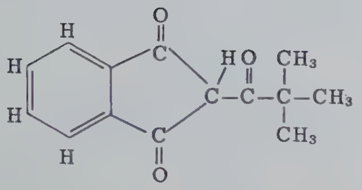
a) For a succinct discussion of synergistic action in general, and postulated mechanisms, etc., consult: Refs. 353,2231,3037,1597.

b) A sharp limitation of the synergistic action of piperonyl cyclonene with pyrethrins is reported from tests conducted by spraying mosquitoes in flight and Sitophilus granarius on residual films from oil solution, when the synergist and pyrethrins were present in equimolecular proportions. This point may be termed the limiting relative potency. 249

c) Enhanced the action of pyrethrum dusts vs. Periplaneta, Blattella; 0.1% pyrethrins + 1% piperonyl cyclonene brought immediate "flush," rapid "knockdown" and complete, fast kill of the insects. 824

148

2-PIVALYL-1, 3-INDAN(E)DIONE (Pival®; Pivalyl Valone; Pivalyl indan(e)dione; 2-tert.-Butyl-1, 3-indan(e)dione;) tert.-Butylvalone.)



Molecular weight 230.252

GENERAL [Refs.: 1793,2231,353,2120,129,1741,2862,1801,2741,149,919,917,207,1510,2024,992,1832,2184,628]

The insecticidal properties of this compound (as of its close relative, 2-isovaleryl-1,3-indandione) were reported first in 1942.2-Pivalyl-1,3-indandione is one of a group of compounds (namely the 2-acyl substituted 1,3-indandiones) which contains members highly toxic to mammals and which are used both as rodent-killing baits and therapeutically, because of their strong anti-blood-coagulant properties, in which they resemble coumarin and its derivatives. 2-Pivalyl-1,3-indandione manifests a very high contact toxicity for Musca domestica, for animal lice and their eggs and (on the basis of screening tests) a high order of effectiveness against ticks, fleas, and adult mosquitoes.

The 1,3-indandiones, acyl-substituted at position 2, show increasing toxicity for Musca with increasing substituent carbon chain length from C_2 through C_5. Thereafter, with increasing length of chain, toxicity for Musca declines as it does also with aryl substituents. Virtually all the comments to be found in this work for 2-isovaleryl-1,3-indandione (Valone®), q.v., are applicable with minor modifications for 2-pivalyl-1,3-indandione. 2-Pivalyl-1,3-indandione is the only member of a long acyl-substituted series of 1,3-indandiones which is more toxic than Valone®.

While intensely toxic for Musca as contact spray, the present compound (like the other acylated 1,3-indandiones) with an insecticidal action approaching that of the pyrethrins does not act fast enough for use alone in contact sprays. It may, however, replace the major part of the pyrethrins, particularly in the more concentrated formulations, leaving a sufficient amount of pyrethrins to insure rapid "knockdown" or paralysis of flies.

2-Pivalyl-1,3-indandione has been reported as more toxic than DDT for Pediculus humanus corporis, yielding a "knockdown" of exceptional rapidity, but being apparently unsafe for human skin. Furthermore, it does not resist washing when used as a clothing treatment.

Cereal baits for rodents prepared with 2-pivalyl-1,3-indandione resist insect infestation and mould growth. As a rodenticide, Pival® is employed as a 0.5% powder used in baits at a concentration of 0.025%, being useful against Norway rat, roof rats and mice.

Pival®, experimentally fed to rabbits, has been reported to act systemically to kill the body lice infesting the treated animals. Ingestion of a single dose of 2.5 mg/k, or daily doses of 0.1 mg/rabbit, is said to protect from body lice.

PHYSICAL, CHEMICAL

A bright yellow crystalline solid with a very slight odor; m.p. 108.5-110.5°C; virtually insoluble in water; soluble in dilute alkalis and ammonia, yielding yellow salts; prepared by the reaction of pinacolone with diethyl phthalate.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) 2-Pivalyl-1,3-indandione is a much more effective poison in small daily dosages than in single large doses. 207
   Vitamin K_1 (2-methyl-3-phytyl-1,4-naphthoquinone, Mephyton) is a more effective intravenous antidote 628
   than vitamin K (tetrasodium salt of 2-methyl-1,4-naphthohydroquinone diphosphoric acid, a synthetic
   vitamin K compound).
   b) Oral administration in olive oil; Comparative toxicity:

1741

Animal	2-Pivalyl-1,3-indandione			2-Isovaleryl-1,3-indandione			2-Propionyl-1,3-indandione		
	Subjects	Dosage (mg/k)	% Mortality	Subjects	Dosage (mg/k)	% Mortality	Subjects	Dosage (mg/k)	% Mortality
Rat	4	100	0	5	100	20	10	300	0
Rat	5	150	80	8	200	100	5	400	80

b) Oral administration in olive oil; Comparative toxicity: 1741

Animal	2-Pivalyl-1,3-indandione			2-Isovaleryl-1,3-indandione			2-Propionyl-1,3-indandione		
	Subjects	Dosage (mg/k)	% Mortality	Subjects	Dosage (mg/k)	% Mortality	Subjects	Dosage (mg/k)	% Mortality
Rat	3	200	100	6	300	100	8	500	75
Rat	3	400	100	—	—	—	9	1000	100
Rabbit	3	100	33	4	100	0	—	—	—
Rabbit	3	150	33	3	150	67	—	—	—
Rabbit	3	200	100	3	200	100	—	—	—

Minimal Daily Doses producing at least 50% Mortality in Rats in 7 days: 2741

Indandione	Daily Dose (mg/k)	Total Dose (mg/k)	% Mortality
Pivalyl	5	25	67
Pivalyl Fe^{++} salt	5	25	83
Isovaleryl	10	50	67
Isovaleryl Fe^{++} salt	10	50	92
Diphenyl acetyl	0.1	0.5	39
Diphenyl acetyl Fe^{++} salt	1.0	5	100
Phenyl acetyl	5	25	92
Acetyl	10	50	50
Benzoyl	10	50	0

c) Dog; oral administration by capsule or stomach tube: 207

Number Subjects	Dosage (mg/k)	No. Dead/ No. Treated	Remarks
2	25	0/2	Recovery of 1 treated and 1 untreated with vitamin K_1.
4	75	1/4	Death in 24 hrs.
2	100	2/2	Death on 3rd and 8th days respectively.
1	25	1/1	As 0.5% Pival® 5 g suspended in 5% acacia-water; dead in 22 days.

(1) Signs, symptoms, etc., in animals receiving single oral doses:

Rats, Rabbits: Labored respiration, progressive muscle weakness, hyperexcitability, pulmonary congestion, venous engorgement, death with heart in systolic standstill; in those dying in 1-2 hrs. after single dose: Petechial haemorrhage in lungs. 1741

Dogs: Gross signs of systemic toxicity: Weakness, anorexia, bleeding at sites of venipuncture; at the 100 mg/k level: Salivation, vomiting, bloody mouth fluid, blood in feces, progressive weakening (with apparently increased muscle tonus) until death. 207

Post mortem: High incidence of sub-capsular and cortical infarcts of kidneys, gastrointestinal irritation, lung haemorrhage. Most of those dying in the experimental period showed some vascularization (or haemorrhage) of the brain and its coverings.

"Fine" symptoms: Progressive lengthening of the prothrombin and coagulation times for dogs at all dosages, with a slow progressive return to normal in survivors.

2) Subacute toxicity; Dogs: 207

a) Ten dogs (2 as controls), 8 receiving Pival® in the diet at 0.025% or 2.5 mg/k/day:

(1) 2 dogs, receiving Pival® as above until death, perished respectively on the 7th and 13th experimental day having received 15 and 32.5 mg/k respectively.

(2) 2 dogs, treated as in (a) until 17.5 mg/k Pival® had been taken and having elevated prothrombin and coagulation times, were taken off the drug but left otherwise untreated; both succumbed within a week with signs similar to those in animals dead of acute doses plus labored respiration, tremors, extensor spasms, coma. Autopsy findings were as in subjects acutely poisoned.

(3) The remaining dogs were carried to recovery after receiving 17.5 mg/k of Pival® and having elevated prothrombin and coagulation times, by administration of Vitamin K_1 (vitamin K synthetic (Synkayvite Roche)).

b) Rats (10), receiving 5 mg/k for 5 consecutive days: 6 dead at 5-8 days from the initial feeding. 628,207

3) Toxicity: Summary:

a) Pival® is an effective anticoagulant whose effects are cumulative as shown by continuous rise (with dosages) of prothrombin and coagulation times.

b) More effective poison in small daily than in single large doses.

c) Acute oral LD is an order of 75-100 mg/k in dogs; subacute LD = ca. 15-35 mg/k given at 2.5 mg/day/k.

d) Death is due mainly to haemorrhagic manifestations.

4) Pharmacological, pharmacodynamical, physiological, etc.; higher animals. 851

a) The comments to be found under 2-Isovaleryl-1,3-indandione apply equally for 2-Pivalyl-1,3-indandione. Anticoagulant activity equal to that of dicoumarol.

5) Hazard for wildlife:
Indubitably hazardous if wild mammals are exposed to baits or preparations designed for rodent control. Used as a rodenticide in baits as Pival® 0.5% powder at 0.025%; kills by anti-coagulant activity. 129

6) Toxicity for insects:

a) Speaking in general of 1,3-indandione compounds: Those with an active methylene between two oxo-groups as the dominant functional group are toxic to insects. Activity is enhanced by acylation of the active methylene group at position 2.

b) Appropriate data for Pival® may be found under 2-Isovaleryl-1,3-indandione, q.v., and the comments there given are apropos for Pival®. Data (among other things) give toxicity values for *Musca domestica*.

c) Comparative effectiveness of 2-Pivalyl-1,3-indandione and other newer insecticides as spot treatments for *Haematopinus eurysternus* on cattle when used as emulsions and wettable powders: 2862

Insecticide	Concentration (%)	% Mortality (24, 48 Hrs.)	Weeks Effective
2-Pivalyl-1,3-indandione	1.0	100	3
"	.5	100	2
"	.25	100	2
"	.1	100	2
"	.05	100	2
DDT	0.5	100	4
"	.25	100	3
Toxaphene®	.5	100	4
Strobane®	.5	100	4
Malathion	.5	100	2
"	.05	100	1
Parathion	.05	100	3
"	.01	100	3
"	.005	25	0
Chlorthion®	.25	100	1
Dipterex®	.25	100	1
"	.1	100	0
Bayer 21/199	.25	100	2
"	.2	100	2
"	.1	100	1
"	.05	100	1
Diazinon	.25	100	2
"	.1	100	2
"	.05	100	1
"	.01	95	1
"	.005	25	1
"	.002	5	1
Pirazinon	.25	100	3
EPN®	.05	100	1
"	.01	100	1
"	.005	100	1
"	.002	25	0
Tetraethyl dithiopyrophosphate	.05	100	1

d) 2-Pivalyl-1,3-indandione; effect on body louse of man, *Pediculus humanus corporis*, after feeding on treated (by oral administration) rabbit host: 149

(1) Minimum effective dose in daily diet of rabbit to prevent louse reproduction = 0.15 mg/k; young nymphs fed twice per day on such hosts died within 3 days.
(2) At 0.125 mg/k to the host, ca. 50% of young lice became mature and a few laid viable eggs.
(3) Mortalities were higher for ♀♀ lice given a single meal on hosts receiving 0.15, .175, .2 mg/k.
(4) Older nymphs showed decrease in susceptibility to 2-pivalyl-1,3-indandione.
(5) Toxicity of host's blood persisted 3 days after cessation of the drug administration.
(6) One rabbit (receiving varying amounts over 8 months) died; no lesions were attributable to the drug on autopsy.

e) Screening tests: Consult Ref. 1801.

7) Pharmacological, pharmacodynamical, physiological, etc.; insects:

a) The remarks given for 2-Isovaleryl-1,3-indandione, q.v., are applicable to 2-Pivalyl-1,3-indandione. 2600,2599

149

PLANTS, INSECTICIDAL:

FAMILIES AND GENERA OF PLANTS OF KNOWN OR REPUTED INSECTICIDAL SIGNIFICANCE:

[after 977] also see Refs.: 2832,298,542,912,1157,1347,1379,1397,1408,1466,1667,1888,1887,2191,2516,2190, 2189,2193,2755

Family, Genus, Species	Comments
1) **AESCULACEAE:**	
a) *Aesculus californica*	Active principle unknown.
2) **ANNONACEAE:**	
a) *Annona reticulata* b) *Annona squamosa*	Ether extractable principle (seeds) is similar in toxicity to rotenone for some insects.
3) **APOCYNACEAE:**	
a) *Haplophyton cimicidum*	Alkaloid effective vs. most insects; as toxic as pyrethrum vs. *Anasa tristis*. Used as dried leaves, water-extract and crude alkaloid.
4) **BORAGINACEAE:**	
a) *Heliotropum peruvianum* b) *Tournefortia hirsutissima*	Heliotropine; active vs. *Pediculus*. Non-toxic dermally; long lasting in cocoa-butter. A general insecticide in Haiti.
5) **CANNACEAE:**	Leaves and stems act like tobacco in greenhouse fumigation.
6) **CELASTRACEAE:**	
a) *Tripterygium wilfordii*	See Wilfordine in this work.
7) **CHENOPODIACEAE:**	
a) *Anabasis aphylla*	See Anabasine in this work.
8) **CLUSIACEAE:**	
a) *Mammaea americana*	Pyrethrin-like principle; seeds most toxic, but other parts (save bark) are toxic in greater or lesser degree to insects.
9) **COCHLOSPERMACEAE:**	
a) *Cochlospermum gossypium*	Kutira gum; increases effectiveness of nicotine vs. *Aphis fabae*.
10) **COMPOSITAE:**	
a) *Chrysanthemum cinerariaefolium*	See Pyrethrins in this work.
b) *Heliopsis scabra*	Scabrin, ether extractable, resembles pyrethrum in action on some insects.
11) **CUCURBITACEAE:**	
a) *Cucurbita pepo*	Leaves rubbed on cattle are said to repel flies; acetone extract of seeds is toxic to mosquito larvae.
12) **EUPHORBIACEAE:**	
a) *Croton tiglium*	Seeds used in China; toxic to aphids; acetone extract more toxic than Derris to goldfish; croton resin more toxic to goldfish than rotenone.
b) *Ricinus communis*	Said to be insecticidal in some varieties and under certain cultural and environmental circumstances.
13) **FLACOURTACEAE:**	
a) *Ryania speciosa*	See *Ryania*, Ryanodine in this work.
14) **FAGACEAE:**	
a) *Castanea dentata*	Yields a dyeing and tanning agent, repellent to *Popillia japonica*.

Family, Genus, Species	Comments
15) **LABIATAE:**	
a) Ocimum basilicum	Oil of basil; at 50 ppm yielded 95% kill of various mosquito larvae. Contact poison toward Musca, Leptinotarsa, etc.
b) Salvia officinalis	Acetone extractable agent (leaves, roots) yielded respectively 80% and 95% kills of mosquito larvae.
16) **LEGUMINOSAE:**	
a) Haematoxylon campechianum	Extracts repellent to Popillia japonica.
b) Millettia pachycarpa	Ground seeds insecticidal for some; alcohol extracts of roots paralyze Aphis fabae. Rich in rotenone and saponin. Potent piscicide. A contact and stomach insecticide when mixed with soap.
c) Mundulea sericea (= suberosa)	Rotenone (q.v.) bearing; Indian strain toxic; 1 of 2 African strains (smooth bark) is toxic, the rough bark (corky strain) is non-toxic.
d) Pachyrhizus erosus	Seeds insecticidal; piscicidal use is made of the plant in some tropical regions. Promising vs. Aphis fabae and Epilachna varivestis.
e) Tephrosia virginiana	Most toxic samples are somewhat more poisonous than pyrethrum, less poisonous than Derris (q.v.) Promising as a contact spray vs. 5 insect species; active principle is rotenone and/or other rotenoids. Many species of the genus Tephrosia (= Cracca) are insecticidal. See Rotenone in this work.
f) Derris elliptica, D. malaccensis	See Rotenone in this work.
17) **LILIACEAE:**	
a) Amianthium muscaetoxicum	Active principle is toxic for Musca Periplaneta Apis and various grasshoppers (Orthoptera); ineffective vs. aphids and tent caterpillars. Used as powdered bulbs or leaves. Water extracts show slow (but marked) toxicity vs. Leptinotarsa and Periplaneta.
b) Melanthium virginicum	Reputed to be toxic for Musca.
c) Schoenocaulon officinale	See Sabadilla in this work.
d) Veratrum album, V. viride	See Sabadilla in this work.
18) **MELIACEAE:**	
a) Melia azedarach	Active principle is soluble in hot water, alcohol, chloroform, ether. Water extract of berries is slightly toxic to Periplaneta and toxic to Apis mellifera. Leaves (applied to soil) reduce termite attacks. Alkaline extract of berries is effective vs. aphids. Leaf extracts, as sprays on plants, are repellent to locusts.
19) **MYRTACEAE:**	
a) Pimenta racemosa	Bay Rum Tree. Oil is toxic to mosquitoes (larvae). Insecticidal use is made of the plant in Venezuela. On clothing, repels gnats. Attractant for Popillia japonica.
20) **PEDALIACEAE:**	
a) Sesamum indicum	See Sesamin in this work.
21) **RANUNCULACEAE:**	
a) Delphinium consolida	Oil of seeds (as 2% contact spray emulsion) is effective vs. spider mites and aphids but ineffective for some others. Active principle(s) is/are alkaloid(s).
22) **RUTACEAE:**	
a) Phellodendron amurense	Unsaponifiable fraction of oil from fruits is toxic in acetone (but not in kerosene) to Musca. Non-lipid fruit residue is toxic to mosquitoes, Musca, Carpocapsa (larva). Toxic principle is rapid in action and pyrethrum-like or nicotine-like.
b) Zanthoxyllum clavaherculis	Yields asarinin, closely related to sesamin, q.v. Potent synergist for Pyrethrum. Also yields herculin which has for Musca a paralytic and toxic action comparable to pyrethrins.

Family, Genus, Species	Comments
23) **SAPINDACEAE:**	
a) *Sapindus marginatus*	Berries (3 only) are said to protect a bushel of wheat from insect infestation. As powder, or in extracts, repels weevils and other insects from dried comestibles.
24) **SIMARUBACEAE:**	
a) *Ailanthus* sp.	An insecticidal principle is reported from bark, wood.
25) **SOLANACEAE:**	
a) *Duboisia hopwoodii*	See Nornicotine in this work.
b) *Nicandra physalodes*	Insecticidal use in India. Reputed to repel flies from rooms and barns and to eliminate *Trialeurodes vaporariorum* from greenhouses.
c) *Nicotiana* spp. e.g. *N. tabacum*, *N. glauca* etc., etc.	See Nicotine, Nornicotine, Anabasine in this work.
d) *Physalis mollis*	Bruised leaves and stems in sugar solution baits are toxic for *Musca*; active principle is a (?) glycoside which in impure form has been found toxic to *Musca*.
26) **STEMONACEAE:**	
a) *Stemona tuberosa*	Insecticidal use mode of the plant by Chinese. Decoction of dried roots is reputed to be toxic to crickets, weevils and lepidopterous larvae. A 50% alcoholic extract is effective vs. fleas and lice.
27) **UMBELLIFERAE:**	
a) *Carum carvi*	Acetone extract of seed is toxic to mosquito larvae.
b) *Conium maculatum*	Active principle = coniine, an alkaloid related to nicotine.
c) *Coriandrum sativum*	*Oil of coriander*, repellent to *Musca* other flies and screw worms; as 2% emulsion spray kills spider mites and cotton aphids.
d) *Pimpinella anisum*	*Oil of anise*, repellent to gnats, *Musca* and other flies.
28) **VITACEAE:**	
a) *Parthenocissus quinquefolia*	Said to have toxic properties for aphids.

150

PROPYLENE DICHLORIDE (Propylene chloride; 1, 2-Dichloropropane; α, β -Dichloropropane; α, β -Propylene dichloride.)

$CH_3CHCl\,CHCl$ Molecular weight: 112.99

GENERAL (Also consult the general treatment titled Fumigants in this work)

[Refs.: 2120, 353, 2815, 1059, 757, 3199, 3378, 2352, 2916]

A fumigant insecticide and one of the two ingredients of D-D Mixture, q.v., in which role it finds a principal employment. Useful per se in the fumigation of stored grains. Generally employed in mixture with other fumigants. Useful, also, in mixture with dichloropropylene against soil nematodes and widely employed as a solvent. Has some virtue as a vermifuge (anthelmintic) particularly against ascarids. Used in emulsions as a spray for peach trees.

PHYSICAL, CHEMICAL (For sorption ratio on patent flour see Fumigants)

A colorless, flammable liquid of chloroform-like odor; m.p. below -70°C; b.p. 96.4°C; $d^{25°}_{25°}$ 1.159, $d^{25°}_{4°}$ 1.155; $n^{20°}_{D}$ 1.438; v.p. 52 mm Hg at 25°C; soluble in water to the extent of 0.27 parts per 100 parts at 20°C; miscible with most organic solvents; flash point (open cup) 21°C, 71°F; fire point at 38°C; inflammable in concentrations of 3.4% - 14.5%.

a) Formulation: As D-D mixture; as Dowfume EB-5 (7.2% ethylene dibromide + 29.5% propylene dichloride + 63.6% carbon tetrachloride.)

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	860 (600-1220)		2907
Rat	or	LD_{50}	2270 (1930-2660)		2907
Rabbit	or	LD_{50}	1330 (990-1800)		2907
Rabbit	ct	LD_{50}	8750 (8310-9200)		2907
Rat	inh	LC_{50}	9.2 mg/l; 2000 ppm	Death in 4 hours.	480
Mouse	inh	LC_{100}	10.4 mg/l; 2200 ppm	Death in less than 7 hrs. exposure.	1488
Dog (one animal)	or	LD	5.0 cc/k	Death in 3¼ hours.	3378

a) 75 ppm = threshold limit for continued exposure. 56

2) Repeated exposure:

a) Guinea pig: Exposure 7 hr per day at 2200 ppm: Lachrymation, swelling of conjunctiva, corneal discoloration, predisposition to secondary infection; 11 of 16 animals dead at end of 5th exposure. 1492

b) Rat: Exposure 7 hr per day at 2200 ppm: Incoordination, "fall-over," prostration, rapid and shallow respiration, slow recovery; 5 of 20 dead after 5th exposure. 1492

c) Mouse: Exposure 7 hr per day at 2200 ppm: Excitement, hyperactivity, incoordination, prostration; all dead but one before end of 1 exposure. 1492

d) Rabbit: Exposure 7 hr per day at 2200 ppm: Moderate irritation; some fatalities after 2nd exposure. 1492

e) Guinea pig, Rabbit, Rat: Exposure 7 hours per day for 5 days: Well tolerated; loss of weight by rat, Guinea pig; exposure to 1500 ppm well tolerated (some incoordination in rat). 1492

f) No serious effects in dogs exposed 7 hours at 1500 ppm. 1492

g) At 1000 ppm exposure for 7 hr per day for 5 days produced drowsiness in Guinea pigs; rabbits were unaffected; many rats and mice dead after a few hours. 1492

h) Mouse, rat: Exposed at 400 ppm 7 hrs per day, 5 days per week for 128-140 hours total exposure: No ill effects save weight decrease in rats; high mortality in mice. 1490

(1) Young rats, held on low protein rations, were more susceptible than controls; resistance was not enhanced by choline, although dl-methionine and l-cystine + choline, influenced markedly the resistance to the treatment. 1492

3) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:

a) Narcotic in effect, tending to yield liver and other visceral damage. 3199

b) In Guinea pigs exposed at 2200 ppm: Much coagulation and focal necrosis of adrenal cortex; congestion and degeneration of adrenal medulla; fatty degeneration of liver and kidneys. Rats, also, showed liver necrosis of the lobular centers, fatty degeneration of kidney and liver; adrenocortical lipoid depletion. 1526

(1) Lesions reached full development 24 - 48 hours following first exposure;
(2) Hepatic and renal changes regressed more readily than adrenocortical damage.

c) In dogs (dead of oral dosages) pathology included: Hypostatic lung congestion, hyperaemia, friability of liver, kidney and bladder congestion, stomach and respiratory tract haemorrhage. 3340

(1) Microscopic pathology: Passive congestion and cloudy swelling of liver; fat droplet accumulation; bile pigment deposition near central veins; severe passive kidney congestion and nephric tubule degeneration.

d) Hepatomata have been noted in "C_3H" mouse strain subjects exposed to propylene dichloride; hepatomata were similar to carbon tetrachloride-vapor-exposure-induced tumors. 1490

e) After 2 hour exposures at 2000 ppm, 1.5 - 2.9 mg/100 cc may be found in blood; at 1500 ppm 0.6 - 1 cc/100 cc; dogs, exposed 7 hours at 1000 ppm showed 1.5 - 1.6 mg/100 cc in the blood. Propylene dichloride was detectable in the urine (0.2 - 0.7 mg/100 cc). 1488

4) Phytotoxicity:

a) Applied to soil at 290 lbs per acre for fumigation: No damage resulted to various subsequently planted crops. 2304

5) Toxicity for insects:

Insect	Route	Dose	Dosage	Remarks	
Sitophilus oryzae	Fumig	LC_{50}	44 mg/l; LC_{99} 132 mg/l	Exposure 5 hrs, 25°C, empty flask.	156
Sitophilus granarius	Fumig	LC_{50}	118 mg/l; LC_{99} 234 mg/l	" " "	156
Tribolium confusum	Fumig	LC_{50}	40 mg/l; LC_{99} 98 mg/l	" " "	156
Tribolium confusum	Fumig	LC_{50}	(No absorbent 45 mg/1;	In presence of flour 235 mg/1 at 25°C, 760 mmHg.)	1013
Limonius canus (larva)	Fumig	LC_{50}	263.2	Exposure 5 hr, 77°F, in soil.	1958
Limonius californicus (")	Fumig	LC_{50}	263.2		1958

a) Vs. Pyrausta nubilalis; fumigated as larvae in cornstalks with propylene dichloride + carbon tetrachloride 9:1 at 2 lbs per 100 ft^3: 783

Exposure Time (hrs)	Temperature (°F)	% Mortality
44	60 - 70	100
24	60 - 70	100
18	60 - 70	82.5
6	60 - 70	36.8
3	60 - 70	28.5
24	76 - 78	100
18	76 - 78	30.8

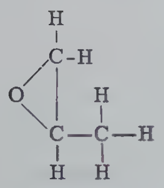
b) More toxic than ethylene dichloride vs. Aegeria exitosa (= Sanninoidea exitosa). 353

c) Inneffective vs. Hylemyia brassicae as a soil fumigant at 1 lb per 100 ft^3, mixed with soil to depth of 8 inches. 659

d) Vs. Hylobius radicis: Less effective than BHC, but gave control. 2813

151

PROPYLENE OXIDE (Propene oxide; 1, 2-Epoxypropane; Methyl oxiane.)



Molecular weight 58.08

GENERAL

A suggested insecticidal fumigant considered useful for soil fumigation; less insecticidal than ethylene oxide, q.v., but superior to carbon disulfide. 2670

PHYSICAL, CHEMICAL

[Refs.: 2120, 1729, 2670]

A colorless, ethereal, flammable liquid; b.p. 34°C; $d_{4°}^{20°}$ .8304, $d_{4°}^{0°}$ 0.859; v.p. 445 mm Hg at 20°C; soluble in water to 40% w/w at 20°C; miscible with alcohols and ethers; quite stable in aqueous solution; explosive limits in air at 2.1% - 21.5% v/v; CO_2 11:1 (w/w), 8.3:1 (v/v) is required to reduce flammability limits.

TOXICOLOGICAL

1) Acute toxicity to higher animals:

Rat	inh	LC	9.5 mg/l 4000 ppm	Exposure 4 hours.	2910

a) No human hazards or injury have been reported. 365

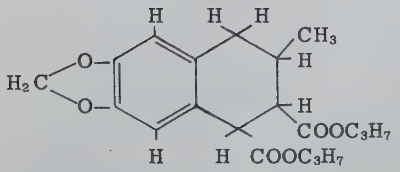
2) Toxicity for insects:

Insect	Route	Dose	Dosage (mg/l)	Remarks	
Sitophilus granarius (adult)	Fumig	LC_{50}	25	Exposure 5 hrs, 25°C, empty flask.	2816,156
Sitophilus granarius (")	Fumig	LC_{99}	41	" " " .	2816,156
Tribolium confusum (")	Fumig	LC_{50}	32	" " " .	2816,156
Tribolium confusum (")	Fumig	LC_{99}	52	" " " .	2816,156
Dacus dorsalis (naked egg)	Fumig	LC_{50}	>87.4	Exposure 2 hrs, 71°-80°F, empty vessel.	255
Dacus dorsalis (larva)	Fumig	LC_{50}	18.5	" " " .	255
Dacus dorsalis (")	Fumig	LC_{95}	28.0	" " " .	255

a) Reported to be useful in vacuum fumigation of spices, killing insects and mold spores in these products. 1911

152

n-PROPYL ISOME (Di-n-propyl-2-methyl-6, 7-methylenedioxy-1, 2, 3, 4-tetrahydro-naphthalene-3, 4-dicarboxylate; Di-n-propyl maleate-isosafrole condensate.)



Molecular weight: 362.408

GENERAL

(Also consult the section titled Synergists, Synergism.) [Refs.: 3041, 2120, 2590, 3137, 1801]

A synergist which potentiates the toxic action of pyrethrins, allethrin, rotenone, and Ryania. Toxicity and hazard to mammals are so low that it is approved for use in household aerosols and in meat packing rooms. No synergism with DDT or nicotine.

PHYSICAL, CHEMICAL

A viscous, oily orange-colored liquid; non-distillable; b.p. 170°-275°C at 1 mm Hg; d 1.14; $n_D^{20°}$ 1.51-1.52; virtually insoluble in water; slightly soluble in petroleum hydrocarbons; soluble in alcohol, ketones, ether, aromatic hydrocarbons, glyceride oils; heat stable; hydrolyzes in strongly alkaline media.

a) Formulations: In petroleum oils with ethylene glycol monobutyl ether as mutual solvent; as emulsifiable concentrates; dusts; aerosols.

TOXICOLOGICAL

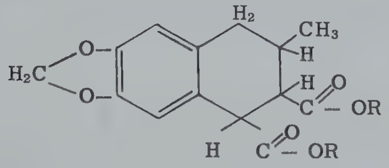
1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD_{50}	ca 15,000		1951
Rabbit	ct	LD_{50}	> 375	Applied as a 4% solution.	1952

2) Chronic toxicity:

a) Rats, receiving 5000 ppm in the diet for 17 weeks, have shown no tissue damage. 1953

3) Synergistic action of n-propyl isome and some of its derivatives with pyrethrins vs. Musca domestica: 3041

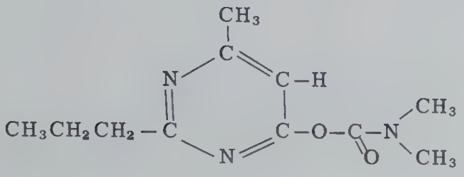


R	Ratio to Pyrethrins	% Mortality Above That Given By Equivalent Pyrethrin Alone
C_2H_5	20	+ 57
$n\text{-}C_3H_7$ (n-propyl isome)	20	+ 74
$n\text{-}C_4H_9$	20	+ 67
$C_6H_5CH_2$	10	+ 64
C_6H_{11}	40	+ 73
CH_2CH_2Cl	20	+ 64
CH_2CH_2SCN	40	+ 38
$CH_2\underbrace{CHCH_2CH_2CH_2}_{O}$	20	+ 41

a) Sharp limitation of insecticidal action is reported when present with pyrethrins in equimolecular proportions, as tested against mosquitoes in flight and Sitophilus granarius exposed to residues of oil film deposits. This point has been called the limiting relative potency. 249

153

2-n-PROPYL-4-METHYLPYRIMIDYL-(6)-DIMETHYL CARBAMATE (Pyramat; G-23330.)



GENERAL (Also consult: Dimetan, Isolan, Pyrolan) [Refs.: 1384, 1317, 2231]

A carbamic acid ester of strong insecticidal power. Kills Musca domestica rapidly with a swift paralytic ("knockdown") action. Of promise as a contact poison, but not successful as a residual toxicant. See the general section in this work titled Carbamates, Carbamic Acid Esters. Reported to be surpassed only by pyrethrins, allethrin, cyclethrin and furethrin in swiftness of action against flies. Feebly toxic for mammals. Intensely toxic for Musca of even the most insecticide resistant biotypes.

PHYSICAL, CHEMICAL [Refs.: 1384, 1317]

A viscous straw-colored liquid; readily soluble in most organic solvents; a derivative of pyrimidine.

TOXICOLOGICAL

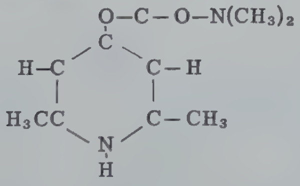
1) Acute toxicity for higher animals:

Rat	oral	LD_{50}	ca. 200 mg/k	1384

2) Toxicity for insects:

a) Among the dimethyl carbamates of pyrimidine, pyridine, pyrazine and pyridazine may be found substances of good insecticidal action and which have a potent neurotoxic effect on insect nerve systems. These substances are, moreover, potent inhibitors of insect choline esterase, a property on which the insecticidal power is believed ultimately to rest. 1317 2231

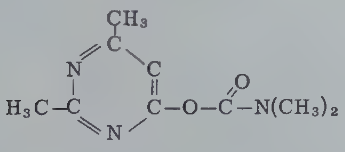
(1) The dimethyl carbamates of 2-, 3-, or 4-hydroxypyridines are relatively feeble insecticides until there are introduced into the molecule certain alkyl groups, whereupon strongly insecticidal compounds appear, for example:



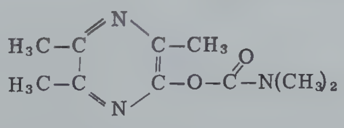
which is active vs. DDT-R flies at a deposit rate of 1 μg/cm².

Condensation of the pyridine with an aromatic nucleus to yield the dimethyl carbamates of quinoline and quinaldine eliminates all toxic action vs. Musca.

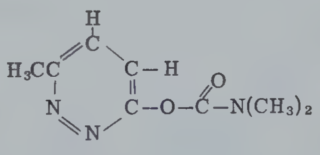
(2) The dimethyl carbamates of pyrimidine and pyrazine show good insecticidal action vs. Musca at deposit rates of 0.1 mg/cm². Pyramat is such a substance. The dimethyl carbamates of pyridazine are inactive, for example:



Active

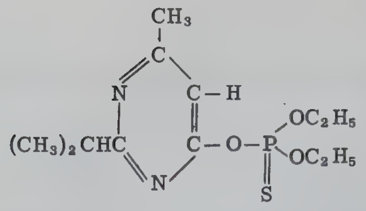


Active



Inactive

(3) Replacement of the dimethyl carbamate of the dimethyl carbamic acid esters of pyrimidine leads to potently insecticidal substances of which Diazinon, q.v., is an example; this substance (in contrast with the carbamates) is active vs. lice and mites.



(Diazinon)

(4) Pyramat in control of Musca domestica (DDT-non R biotype); field applications in dairy barns:

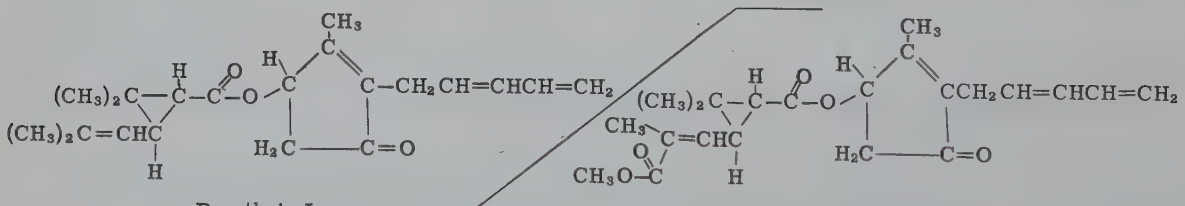
Barn	Treatment	Date	Days of Control Obtained
2	Pyramat 2%	June 17	21
4	Pyramat 1%	June 17	2
2	Pyramat 1% + Methoxychlor 1%	July 29	21

154

PYRETHRINS I, II; PYRETHRUM (Cinerolone, Pyrethrolone esters of mono- and di-chrysanthemum carboxylic acids; Dalmatian Insect Flowers; Powder or extracts of Chrysanthemum cinerariaefolium)

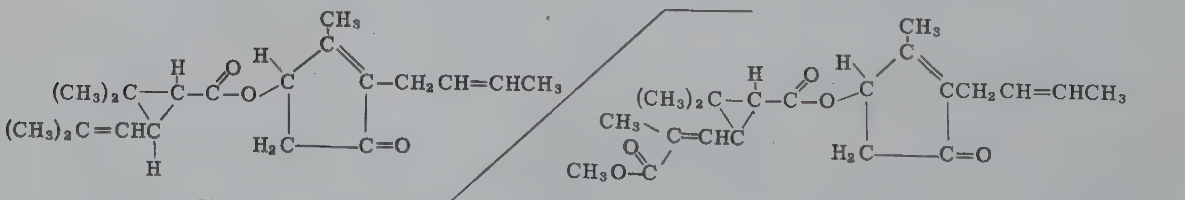
N.B.

By pyrethrins I, II, is to be understood: For pyrethrin I, the esters pyrethrin I and cinerin I; for pyrethrin II: 1897
The esters pyrethrin II and cinerin II, occurring in various proportions in the natural product, pyrethrum, 2956,1893
depending on the strain of Chrysanthemum cinerariaefolium, locale and circumstances of cultivation, tech- 1894,1896
niques of extraction and condensation.



Pyrethrin I

Pyrethrin II



Cinerin I

Cinerin II

Thus, it is evident that the active principles of extracts of pyrethrum flowers are: For pyrethrin I and cinerin I, esters respectively of the alcohols pyrethrolone and cinerolone and chrysanthemum monocarboxylic acid; for pyrethrin II and cinerin II, esters respectively of pyrethrolone and cinerolone and chrysanthemum dicarboxylic acid monomethyl ester.

GENERAL (Also consult Allethrin, Cyclethrin, Furethrin, Synergism) [Refs.: 353, 2231, 2815, 757, 1059, 2226, 2120, 129, 151, 977, 851, 1801]

The insecticidal principles of pyrethrum are among the most useful and safe of all insect toxicants being noted for an extraordinary rapidity of action and a wide "spectrum" of activity to diverse insect species. The complex of substances which constitutes "pyrethrum," in the broad sense, occurs in nature in the genus Chrysanthemum

(= Pyrethrum) (Compositae), and particularly in Chrysanthemum cinerariaefolium and Chrysanthemum coccineum, plants whose insecticidal properties have long been known. Pyrethrin content ranges from 1.3 - 3% (flowers from Kenya) 1% (flowers from Japan) 0.7% (flowers from Dalmatia). The active principles reach their greatest concentration in mature flower heads (ca one-tenth as much is present in the stems) with the achenes being the principal site of concentration. The active principles have been synthesized and a series of purely synthetic analogues elucidated as well. These are potent, direct contact insecticides, producing rapid paralysis, but lacking in persistent or residual properties. The pyrethrins yield the most convincing evidences of synergism with various compounds.

PHYSICAL, CHEMICAL

[Refs.: 2956, 462, 463, 1396, 652, 1398, 250, 653, 2923, 1894, 1895, 1896, 1897, 3286, 689, 2752, 651, 1205, 1206, 251, 668, 2754, 2467, 3335]

Pyrethrins I and II are viscous, brown, liquid oleoresins; b.p. I = 170°C at 0.1 mm Hg, with decomposition; II = 200°C at 0.1 mm Hg, with decomposition; n_D: I = 1.5192 at 18°C; II = 1.529 at 21.5°C; both are virtually insoluble in water, but are soluble in many organic solvents, for instance alcohol, petroleum ether (II less than I), kerosene, carbon tetrachloride, ethylene dichloride, nitromethane; rapidly oxidized and inactivated in air; decomposed by exposure to light with loss of insecticidal activity; the constituents: Pyrethrolone = d-2-cis-(penta-2',4'-dienyl)-3-methyl-cyclopent-2-en-4-ol-1-one (d-cis-penta-2,4-dienylrethrolone); cinerolone = d-2-cis-(but-2'-enyl)-3-methyl-cyclopent-2-en-4-ol-1-one (d-cis-but-2-enylrethrolone) b.p. respectively 110°-112° at 0.1 mm Hg, 120°-124° at 1 - 2 mm Hg; pyrethrolone and cinerolone exist in optically active and racemic form; chrysanthemum monocarboxylic acid (chrysanthemic acid) = 2,2-dimethyl-3-isobutylene cyclopropene-1-carboxylic acid b.p. 135° at 12 mm Hg; chrysanthemum dicarboxylic acid monomethyl ester (pyrethric acid) b.p. 140°C at 0.5 mm Hg; the two acids may exist as stereo- and geometric-isomers, for example dl-transchrysanthemic acid (m.p. 54°C) dl-cis-chrysanthemic acid (m.p. 115°-116°C) l-trans-chrysanthemic acid (m.p. 19°C) have been synthesized in crystalline form; d-trans-chrysanthemic acid (m.p. 17°-21°C) has been identified with the acid of natural pyrethrins and d-cis chrysanthemic acid (m.p. 40°-42°C) and l-cis-chrysanthemic acid (m.p. 41°-43°) have been recovered from racemates; the naturally occurring form of pyrethric acid is also d-trans.; flowers (in the unground state) are more stable in air and light than the pulverized product; antioxidants usefully protect insecticidal residues of pyrethrins, for instance pyrocatechol, pyrogallol, hydroquinone; benzene-azo-β-naphthol exercises a protectant effect in sunlight; most of the insecticidal action is destroyed by minor changes in the pyrethrin or cinerin molecules.

a) Formulations: Dusts (ground flower heads) in non-alkaline carriers; aerosols in volatile liquids; combined with synergists in aerosols; extracts as sprays in suitable solvents.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) Average LD_{50} oral (acute) for all animals tested = 1500 mg/k, the chronic MLC = 500 ppm. 1949

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	ip	LD_{100}	200	Given in petroleum oil.	2827
Mouse	ip	LD_{50}	40	Pyrethrin II in lauryl glycol.	1127
Mouse	ip	LD_{100}	60	" "	1127
Mouse	ip	LD_{50}(ca) = LD_{66}	240	Pyrethrin II in sesame oil; death in 21-141 min	1971
Mouse	ip	LD_{100}	>480	" "	1951
Mouse	ip	LD_{83}(ca)	480	Pyrethrins I, II in sesame oil.	1951
Rat	or	LD_{50}	820(680-1000)	In a 20% oil base.	478
Rat	or	LD_{50}	1870(1340-2600)	"	478
Rat	or	LD_{50}	ca 1500		1949
Rat	ip	LD_{90}	200	In petroleum oil.	2827
Guinea Pig	ip	LD_{90}	200	"	2827
Guinea Pig	ip	LD_{50}	100-150		1971
Guinea Pig	ip	LD_{100}	120	Pyrethrin I; in lauryl glycol.	1127
Guinea Pig	or	LD_{50}	1500	Death in 48 hrs.	1971
Dog	iv*	LD	6-8		536
Fish	Medium	Toxic Dose	20 ppm (0.2 ppm pyrethrins)	As pyrethrum flowers.	174,939
Carp	Medium	Harmful	2 ppm	Affects movements. As pyrethrum flowers.	174,939
Carp	Medium	LC	5-10 ppm	Paralysis before death. "	174,939
Trout (fingerling)	Medium	Disabling Dose	5-10 ppm (0.1 ppm pyrethrins)	"	3175
Acellus aquaticus (Crustacea)	Medium	LC	0.002 ppm	As pyrethrum flowers.	3175

* intravenous

2) Sub-acute and chronic toxicity for higher animals:

a) Rats: Received 1000 ppm in diet for 2 years without tissue pathology. 54

b) Rats: Received 5000 ppm in diet: Tissue damage and gross signs in one series, but not in another. 54

c) Rabbits: Dermal applications at 200-400 mg/k gave toxic signs. 1971

d) Guinea Pigs, Rats: Survived 480 mg/animal, with diarrhoea as only symptom. 1971

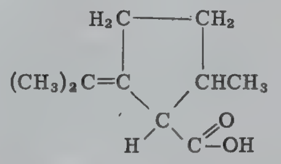
e) Rabbits: Survived, with permanent tremor and spastic incoordination, 240 mg/k of pyrethrin II. 1971

f) Irritating to eyes and mucous membranes; dermatitis in some hypersensitive human subjects. Allergic reactions in sensitive subjects. 2132 851

3) Pharmacological, pharmacodynamical, physiological, etc.; higher animals:
  a) Reported to be more toxic to man by inhalation than by other routes, with pyrethrin II being less toxic than pyrethrin I. 2221
    (1) Sternutatory and bitter in taste when aerosols are overused. 851
  b) Symptoms of acute poisoning are: Hyperexcitability, incoordination, convulsions, with death in respiratory paralysis. Oral toxicity is low for mammals and is stated to present less of a hazard than pyrethrin solvents. Chronic poisoning is said to be unlikely. 851
  c) In mice, the threshold of a peculiar convulsant action, "dancing in place", is reported as 20 mg/k for pyrethrins I and II. 1971

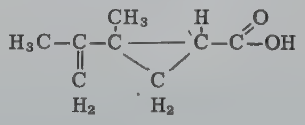
4) Phytotoxicity:
  a) Apparently non-phytotoxic; no reports of phytotoxicity with pyrethrins, as such, appear in the "literature". Solvents of pyrethrins, improperly applied, may present a hazard as is the case with many insecticide formulations.

5) Toxicity for insects:
  a) Pyrethrolone and cinerolone (keto-alcohol moieties) and the chrysanthemum mono- and di-carboxylic acid moieties of the pyrethrins in uncombined form are non-toxic to insects. 934,2956 2955,3058
    (1) No esters compare with the naturally occurring esters in general insecticidal activity. 2956,1443
    (2) Esters of acetic, isobutyric, undecylenic, malonic, benzoic, o-methoxybenzoic, cinnamic, geranium, camphor ester, β-fencholic, citronellic, piñon, crotonic, dichloroacrylic acids are all inactive. 2956
    (3) Esters of pulegenic acid with pyrethrolone and cinerolone are weakly active insecticides:

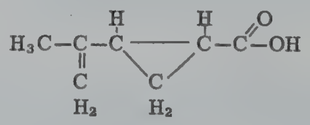


= pulegenic acid;

and of all tested modifications of the acid moiety, esters of the following acids with pyrethrolone, cinerolone proved the most active:



;



  b) Structure and Insecticidal Activity: 934
    (1) Relative toxicity of pyrethrum components for Musca domestica: 1147,2231

Component (As kerosene sprays)	[Ref. 1147] Relative Toxicity (Pyrethrin I = 1)	[Ref. 1147] Ratio	[Ref. 2231] Relative Toxicity (Pyrethrins = 1)
Pyrethrin I	1.0	1	2.0
Pyrethrin II	4.3	0.25	0.46
Cinerin I	1.4	0.69	1.38
Cinerin II	5.8	0.17	0.35
d-cis-Cineronyl-d-trans-chrysanthemate	---	---	0.67
l-cis-Cineronyl-d-trans-chrysanthemate	---	---	1.22
d-cis-Cineronyl-l-trans-chrysanthemate	---	---	0.17
l-cis-Cineronyl-l-trans-chrysanthemate	---	---	0.12
Isohydropyrethrin I*	2.0	0.5	1.0
Isohydropyrethrin II *	Non-toxic at level used		Non-toxic at level used
Isohydrocinerin I*	3.6	0.35	0.56
Isohydrocinerin II *	Non-toxic at level used		Non-toxic at level used
Tetrahydropyrethrin I*	>16	0.06	<0.06
Dihydrocinerin I*		0.08	---

J.E.E. 578, 1947

Error in Laforge's paper (personal communication to ME)

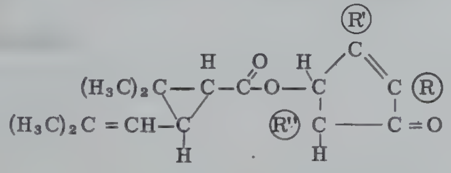
*Hydrogenation of the side chain reduces toxicity appreciably and destroys the characteristic "knockdown" effect.

(2) Relative toxicity of pyrethrins vs. several insect species; as variously reported:

Component	Form	Remarks	Other	
Pyrethrin I	H_2O, suspension spray	1.25 times as toxic as II	(Blattella germanica) LC_{50} 24 hr { I = 10 mg/l II = 12.5 mg/l	1207 Quad
Pyrethrin I	Kerosene spray	1.3 times as toxic as II	(Musca domestica) LC_{50} { I = 65 mg/100 cc II = 85 mg/100 cc	1208
Pyrethrin I	H_2O spray + saponin	10 times as toxic as II	(Aphis rumicis) LC_{50} 24 hr { I = 1 mg/100 cc II = 10 mg/100 cc	3058 Ta H
Pyrethrin I	In miscible oil	Equal in toxicity to II	(Aphis rumicis)	1431 Hart
Pyrethrin I	In heavy mineral oil + H_2O	Equal in toxicity to II	(Tribolium castaneum)	2127 Machin
Pyrethrin I	In alcohol solution + H_2O	Many times more toxic than II	(Tribolium castaneum)	2127
Pyrethrin I	In acetone solution + H_2O	ca equal in toxicity (I & II)	(Musca domestica) Topical & Sprays	1431 Hart "
Pyrethrin I	Kerosene spray	Yielded in 24 hrs twice the mortality given by II	(Musca domestica)	3005 S
Pyrethrin II	Kerosene spray	10 min. "knockdown" 3.5 times that of I	(Musca domestica)	3005 Sullivan
Pyrethrin I	Kerosene solution	Slightly greater mortality than with II	(Periplaneta americana) { Topical LC_{50} 24 hr I = 1.0 mg/l II = 1.5 mg/l	2178 Mc
Pyrethrin II	Kerosene solution	More rapid "knockdown" than I	(P. americana) { 50% "KD" 30 min. II = 1.0 mg/l I = 1.5 mg/l	2178
Pyrethrolone Chrysanthemum-mono-carboxylic acid Chrysanthemum dicarboxylic acid		Non-toxic at 0.2 g/100 cc sprays, H_2O + saponin	(Aphis rumicis)	3058 Tatt el
Pyrethrin I	(Topical Administration)	2.6 times as toxic as II	(Phaedon cochlearis)	3227 Ward.
Cinerin I	(Topical Administration)	2.5 times as toxic as II		
Pyrethrolone Cinerolone	esterified with chrysanthemic acid (monocarboxylic)	4.3 4.0 } times as toxic as pyrethric acid ester vs. Musca as are kerosene sprays.		1147

(3) Toxicity of synthetic "pyrethroids" vs. Musca domestica; after [Ref. 2231] quoting [Refs.: 1148, 1161, 1159, 1162, 2752] :

JEE 44.70 JEE 45,945



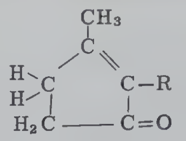
R	R'	R''	Configuration (Acid)	Relative Toxicity Pyrethrins = 1		
$CH_2CH=CHCH_3$	CH_3	H	d-trans	1.48	22	
$CH_2CH=CH_2$	"	"	d-trans	6.64	100	
$CH_2CH_2CH_2CH_3$	"	"	d-trans	0.17	3	
$CH_2C(CH_3)=CH_2$	"	"	d-trans	3.46	52	52
$CH_2CH=C(CH_3)_2$	"	"	d-trans	0.21	3	
$CH_2CH_2CH=CH_2$	"	"	d-trans	0.61	9	9
$CH_2\underbrace{C=CHCH=CH}_{O}$	"	"	d-trans	1.92		55
$CH_2\underbrace{C=CHCH=CH}_{O}$	"	"	dl-cis-trans	1.11		
$CH_2CH=CH\ CH_3$	"	"	dl-cis	0.38		
$CH_2CH=CH\ CH_3$	"	"	dl-trans	0.40		
$CH_2CH=CH_2$	"	"	dl-cis	1.8		
$CH_2CH=CH_2$	"	"	dl-trans	1.81		
$CH_2C\equiv CCH_3$*	"	"	dl-cis-trans	0.73		
$CH_2CCl=CH_2$	"	"	dl-cis-trans	1.56		
CH_2* $CH=CHCl$	"	"	dl-cis-trans	1.42		
$CH_2CH=CCl\ CH_3$	"	"	dl-cis-trans	0.21		
CH_3	"	"	dl-cis-trans	0.40		
CH_2CH_2	"	"	dl-cis-trans	0.94		
$CH_2CH=CH_2$	"	"	dl-cis-trans	3.24		
$CH_2CH=CH_2$	"	$CH_2CH=CH_2$	dl-cis-trans	0.41		
$CH_2CH=CH_2$	C_6H_5	H	dl-cis-trans	0.43		

$CH_2CH=CH.CH=$

$CH_2CH=C$

Summary: dl-trans esters slightly more toxic than d-cis-trans esters.
l-trans esters much less effective.
l-cis esters probably inactive.

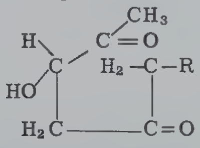
(4) Relative toxicity of Cinerin I analogues for Musca domestica: 1148,2752



R = various side-chains attached to a cyclopentenolone nucleus; effects of side-chain saturation at keto position and other changes, such as chain length, branching, stereochemical, etc.

R	Chrysanthemum Mono-carboxylic Acid, Configuration			Relative Toxicity	
(1) - $CH_2CH = CHCH = CH_2$ (pyrethrolone)	d-trans (natural)		33	1	
(2) - $CH_2CH = CHCH_3$ (cinerolone)(cis)	"	cis, trans configuration of side chain		0.7	= equal toxicity
(3) - $CH_2CH = CHCH_3$ (")(trans)	"			0.7	
(4) - $CH_2CH = CH_2$	"		100	3.3	
(5) - $CH_2C(CH_3) = CH_2$	"		52	1.7	
(6) - $CH_2CH_2CH = CH_2$	"		9	0.3	
(7) - $CH_2CH = C(CH_3)_2$	"		3	0.1	
(8) - $CH_2CH_2CH_2CH_3$	"		2	0.08	
(9) - $CH_2CH = CHCH_3$	dl-cis			0.2	
(10) - $CH_2CH = CHCH_3$	dl-trans			0.2	
(11) - $CH_2CH = CH_2$	dl-cis			0.9	
(12) - $CH_2CH = CH_2$	dl-trans			0.9	

Summary: Among the above compounds closely related to cinerin I, (2) and (3) differ in cis- and trans-configuration of side chain; (4) esterified with natural dextro-acid is more than 3 times as toxic as (11), (12) esterified with optically inactive acids; esterification of synthetic trans-cinerolone with optically inactive acids (9), (10) reduces mortality to ca. $\frac{1}{3}$ of that yielded when natural acid is used. Toxicity of pyrethrins and cinerins was largely destroyed by side chain saturation in the keto portion of molecule. Replacement of methyl group in 3 position by other groups, for instance phenyl for methyl in the allyl ester, decreased toxicity to $\frac{1}{15}$ th that of the allyl homologue of cinerin I, for Musca. An uncyclized compound:



where R = allyl, esterified with natural chrysanthemum acid, proved less than $\frac{1}{70}$ th as toxic as the corresponding cyclized compound, (4) in the preceding tabulation.

(5) Studies in which the acid component of pyrethrin I and cinerin I, namely chrysanthemum monocarboxylic acid, has been esterified with alcohols other than pyrethrolone or cinerolone have been reported and the products tested against cockroaches. Products of reactions between chrysanthemum acid chloride and various alcohols and phenol have not been toxic enough to warrant further study. Esterification of chrysanthemic acid with 18 aliphatic alcohols (from ethyl to cetyl) and tests of the products against aphids and cockroaches showed lauryl, myristyl and cetyl esters to be almost as toxic as pyrethrins vs. aphids although none had pyrethrin-like action vs. cockroaches. S&R, 19 2957 1443 Harrill, 1939

(6) Compounds derived by esterification of the natural keto-alcohols pyrethrolone and cinerolone with natural dextro-acids (chrysanthemic acid, pyrethric acid) do not differ in toxicity from those prepared from optically inactive keto-alcohols with optically active acids. No difference in toxicity was noted between cinerin I with a keto-alcohol side chain of cis- and a keto-alcohol side chain of trans-configuration. 1147 Gersdorf 654 Crombie/ 1148 Gersdorf 1949

(7) Variations in structure of the acid component; further remarks:

(a) Double bond hydrogenation of pyrethrolone and cinerolone chrysanthemic acid esters decreases toxicity to Musca by $\frac{1}{2}$; "knockdown" persists. 1147

(b) The d-trans esters are the natural esters of chrysanthemic and pyrethric acids; d-trans-chrysanthemates of dl-cinerolone are ca. 3.7 times as toxic as dl-trans-chrysanthemates for Musca; d-cis-cineronyl d-trans-chrysanthemate is 4 times as toxic as d-cis-cineronyl l-trans-chrysanthemate; l-cis-cineronyl d-trans-chrysanthemate is 10 times as toxic as l-trans-cineronyl l-trans-chrysanthemate. Thus, d-trans-esters are more toxic than d-cis-esters; l-trans-esters are much less toxic for insects than d-trans-esters; l-cis-esters are putatively inactive. 1898 1148 2231 934

(c) With respect to "knockdown" properties and toxicity, the structural requirements of the acid component for "knockdown" ability are much less specific than for toxicity, i.e. mortality. "Knockdown" is retained after the esterification of pyrethrins with acids other than chrysanthemum acids, but toxicity is virtually extinguished. 934

(8) The alcoholic component; toxicity, "knockdown":

(a) Cinerolone and pyrethrolone are optically active; the l-cis-cineronyl configuration (as the d-trans-chrysanthemate) is more toxic than the d-cis-cineronyl configuration. Natural cinerolone is in cis-configuration, but the trans-configuration is ca. equitoxic for Musca. 1898

(b) Esters of chrysanthemic acid with the following alcohols and phenols proved inactive in "knockdown" property vs. Blattella germanica: Methyl, amyl, capryl, heptyl and allyl alcohols, 2-methyl Δ -3,4,5,6-heptadienol, ethylene glycol, ethylene chlorohydrin, ethyl lactate, diacetone alcohol, 2957 S&R 1924 acetopropyl alcohol, dextrose, levulose, mannose, phenol, carvacrol, salicyl aldehyde, hydroquinone, monomethyl ether, thymol, orcinol monomethyl ether, pyrocatechol, isoeugenol, o-allyl vanillin, benzyl alcohol, triphenyl carbinol, phenylethyl alcohol, p-methoxybenzyl alcohol, benzhydrol, o-hydroxybenzyl alcohol, methylsantonic acid, hydroxycamphor, hydroxymethylene camphor, cholestrin, methyl mercaptan, thiophenol, ethyl-, allyl-, benzyl- and β-phenylethyl-amines, aniline, p-nitroaniline and o-methoxyaniline.

The following had slight "knockdown" action:
esters of guiacol, eugenol, vanillin, piperonyl alcohol, allylphenyl carbinol, p-isopropylbenzyl alcohol, phenylpropyl alcohol, methyl styryl carbinol, cinnamic alcohol, citronellol, linalool, menthol, geraniol, methyl cyclohexanol, α-terpineol, borneol, sabinol, phytol, benzoin, benzoyl alcohol and dimethyl hexeneolone.

The following proved inactive:
chrysanthemic acid esters of: 3-Methyl,- 3-phenyl-, 2,3-dimethyl-, 3-methyl-2-carbonester, 3-methyl-2-allyl-2-allyl-2-carbonester, 3-methyl-2-propenyl, cyclopentenolones and cyclopentanolones, 3-methyl-2-allyl- and 3-methyl-5-allyl-cyclopentenolones, styryl cyclopentenolone, 3-styryl-cyclopentadiene dicarbonester and benzal cyclopentanolone.

(c) Esterification of chrysanthemic acid with the following yielded compounds less than 0.06 as effective as natural pyrethrins vs. Musca: Furfuryl alcohol, $\alpha\alpha$-dimethyl phenethyl alcohol, 1-(p-tolyl) -ethanol, p-cresol, hydroquinone diester, p-methoxyphenol and 8-quinolinol. 2286

(d) The following are non-toxic to Musca: p-Chlorophenyl dl-cis- and dl-trans-chrysanthemate, p-chlorophenacyl-, p-chlorophenethyl- and 2,2,2-trichloroethyl-dl-trans-chrysanthemate; p-chlorobenzyl dl-trans-chrysanthemate shows moderate toxicity vs. Musca. 1399

(9) Other important structural considerations:

- (a) Position of side-chain unsaturation, for example, d-trans-chrysanthemate of 2-but-2'-enyl-3-methyl-cyclopent-2-en-4-ol-1-one proved 2.4 times as toxic for Musca as 2-but-3'-enyl cyclopentenolone. 1148
- (b) Introduction of a triple bond, as in but-2-ynyl side-chain yielded no change in toxicity. 1159
- (c) Chlorination of cinerolone side-chains brought decrease in toxicity of dl-cis-trans chrysanthemates to $\frac{1}{2}$ that of the unchlorinated analogues. 1159
- (d) Esterification of cinerin I with chrysanthemic acid at position 5, rather than 4, in the cyclopentenolone ring yielded a product ca. 0.12 as toxic as cinerin I. 1890

(10) In summation, it may be said that virtually all structural modification of the pyrethrin or cinerin molecule, whether in the alcoholic or acidic component or moiety, degrades the toxicity and modifies the "knockdown" capacity.

c) Quantitative toxicity; insects:

(1) For several insect species as determined by one investigator: 2219
Menusan, 194

Insect	Route	Dosage (μg/g) For Mortality % Shown of Pyrethrins I, II								
		0%			50%			100%		
		♂	♂♀	♀	♂	♂♀	♀	♂	♂♀	♀
Anasa tristis	Topical	-	2	-	-	7	-	-	26	-
Anasa tristis	Injection	-	4	-	-	10	-	-	25	-
Bombyx mori (larva)	Topical	-	-	-	-	-	-	-	< 0.4	-
Ceratomia catalpae (larva)	Topical	-	0.7	-	-	2	-	-	6	-
Ceratomia catalpae	Injection	-	1	-	-	4	-	-	6	-
Oncopeltus fasciatus	Topical	-	3	-	-	8	-	-	28	-
Periplaneta americana	Topical	2	-	6	4	-	9	6	-	12
Periplaneta americana	Oral	8	-	18	14	-	29	20	-	40
Periplaneta americana	Injection (blood)	1	-	5	3	-	8	6	-	11
Popillia japonica	Topical	-	10	-	-	40	-	-	130	-
Popillia japonica	Injection	-	10	-	-	40	-	-	110	-
Tenebrio molitor	Topical	-	25	-	-	35	-	-	100	-

(2) Observations by various investigators:

Insect	Route	Dose	Dosage	Remarks	
Aëdes aegypti (adult ♂)	Contact Spray	LD$_{50}$	0.5 (.5-1.0) μg/g	As 0.1% w/v solution.	693 David AAB
Aëdes aegypti (" ♀)	Contact Spray	LD$_{50}$	1.0 (1.0-1.5) μg/g	As 0.1% w/v solution.	693 " "
Chaoborus astictopus (winter larva)	Medium	LC$_{100}$	0.33 ppm	Solution sans wetting agent.	768 Deonier &
Chaoborus astictopus (")	Medium	LC$_{99}$	0.2 ppm	"	768
Chaoborus astictopus (")	Medium	LC$_{66}$	0.033 ppm	"	768
Chaoborus astictopus (")	Medium	LC$_{100}$	0.2 ppm	Solution + Na lauryl SO$_4$ wetting agent.	768
Chaoborus astictopus (")	Medium	LC$_{93}$	0.1 ppm	"	768
Chaoborus astictopus (")	Medium	LC$_{63}$	0.033 ppm	"	768
Chaoborus astictopus (")	Medium	LC$_{36}$	0.016 ppm	"	768
Agrotis orthogonia (larva)	Spray	LDeposit$_{50}$	8.2 μg/cm^2		350 Brown, 19
Choristoneura fumiferana (larva)	Spray	LDeposit$_{50}$	0.05 μg/cm^2		350
Cimex lectularius (adult)	Contact Spray	LD$_{50}$	0.02 μg/insect		413 Busvine,
Cimex lectularius (")	Contact Spray	LD$_{50}$	5 μg/g		413 "

(2) Observations by various investigators (Continued):

Insect	Route	Dose	Dosage	Remarks		
Cimex lectularius (adult)	Contact Spray	LD$_{50}$	0.012 μg/insect	Pyrethrins + 2% isobutyl undecylenamide.	413	Brow
Cimex lectularius (")	Contact Spray	LD$_{50}$	3 μg/g	"	413	
Apis mellifera (")	or	LD$_{50}$	0.5 μg/g	At 20°C.	296	Bött ge
Apis mellifera (")	or	LD$_{50}$	5.0 μg/g	At 34.5°C.	296	1944
Heliothis ononis (larva)	Spray	LDeposit$_{50}$	4.0 μg/cm^2		350	Brown
Pediculus humanus corporis	Contact Spray	LD$_{50}$	0.085 μg/insect		413	Brown
Pediculus humanus corporis	Contact Spray	LD$_{50}$	42 μg/g		413	
Pediculus humanus corporis	Contact Spray	LD$_{50}$	0.007 μg/insect	Pyrethrins + 2% isobutyl undecylenamide.	413	
Pediculus humanus corporis	Contact Spray	LD$_{50}$	3.5 μg/g	"	413	
Pediculus humanus corporis	Residue	LDeposit	6 μg/cm^2	On flannel as 50% in oil.	414	Brown
Pediculus humanus corporis	Residue	LDeposit	4.5 μg/cm^2	" 10% " .	414	
Pediculus humanus corporis	Residue	LDeposit	31 μg/cm^2	" in volatile solvent.	414	
Pediculus humanus corporis	Contact Spray	LC$_{50}$ (%)	34%	Commercial; 0.44% pyrethrins in oil at 0.36 mg/cm^2.	414	
Pediculus humanus corporis	Contact Spray	LC$_{50}$ %	3%	Pyrethrins + 2% isobutyl undecylenamide at 0.36 mg/cm^2.	414	
Fannia canicularis (adult)	Topical	LD$_{50}$ 24 hr	♀0.24,♂0.44 μg/fly	In acetone; measured drop test.	1981	Le Wallen
Phaedon cochleariae (adult)	Contact Spray	LC$_{50}$ w/v	.00037%	Application as aqueous sprays + 0.1% sulfonated lorol, 10% acetone in the Potter tower.	935	Elliott
Phaedon cochleariae (")	Contact Spray	LC$_{50}$ w/v	.000305%		935	
Phaedon cochleariae (")	Contact Spray	LC$_{50}$ w/v	.000324%		935	
Macrosiphum solanifolii (adult♀♀)	Contact Spray	LC$_{50}$ w/v	.000541%		935	
Macrosiphum solanifolii (")	Contact Spray	LC$_{50}$ w/v	.000704%	"	935	
Macrosiphum solanifolii (")	Contact Spray	LC$_{50}$ w/v	.00034%		935	
Oryzaephilus surinamensis (adult)	Contact Spray	LC$_{50}$ w/v	.00552%		935	
Oryzaephilus surinamensis (")	Contact Spray	LC$_{50}$ w/v	.00789%	"	935	
Oryzaephilus surinamensis (")	Contact Spray	LC$_{50}$ w/v	.00537%		935	
Plutella maculipennis (larva, last instar)	Contact Spray	LC$_{50}$ w/v	.00899%		935	
Plutella maculipennis (")	Contact Spray	LC$_{50}$ w/v	.00346%	"	935	
Plutella maculipennis (")	Contact Spray	LC$_{50}$ w/v	.005754%		935	
Pliophila casei	Aerosol	LC$_{98}$ 24 hr	50 mg/960ft^3	In dichlorodifluoromethane + sesame oil.	243	Bulinge
Pliophila casei	Aerosol	LC$_{66}$ 24 hr	25 mg/960ft^3		243	
Anopheles quadrimaculatus (larva)	Medium	MLC$_{100}$	0.1 ppm	78% kill at 0.05 ppm.	2020	Lindqu
Musca domestica (adult)	Contact Spray	LC$_{50}$ 24 hr	1.2 $\pm$.14 mg/cc	Standard pyrethrins as acetone: kerosene spray 1:1.	1164	Gersdo
Musca domestica (" ♂)	Contact Spray	LD$_{50}$	31.0 (30-35) μg/g	As 2% w/v pyrethrins in 50/50 odorless distillate + benzene.	693	David
Musca domestica (" ♀)	Contact Spray	LD$_{50}$	38.0 μg/g	"	693	
Musca domestica (adult)	Topical	LD$_{50}$ 24 hr	1.0 μg/fly	Laboratory (non DDT-R) strain, measured drop method.	78	Anon
Musca domestica (")	Topical	LD$_{50}$ 24 hr	1.0 μg/fly	Bellflower (DDT-R) strain, measured drop method.	78	
Musca domestica (")	Topical	LD$_{50}$ 24 hr	2.0 μg/fly	San José (DDT-R) strain, measured drop method.	78	
Musca domestica (")	Topical	LD$_{50}$ 24 hr	2.0 μg/fly	Ontario (DDT-R) strain, measured drop method.	78	
Musca domestica (")	Topical	LD$_{50}$ 24 hr	2.0 μg/fly	Riverside (DDT-R) strain, measured drop method.	78	
Musca domestica (")	Topical	LD$_{50}$ 24 hr	88.1 μg/g	DDT-I R-strain; pyrethrins + piperonyl butoxide 1:10.	373	Bruce Dech
Musca domestica (")	Topical	LD$_{50}$ 24 hr	74.8 μg/g	DDT-W, R-strain; pyrethrins + piperonyl butoxide 1:10.	373	
Musca domestica (")	Topical	LD$_{50}$ 24 hr	65.8 μg/g	DDT-III, R-strain; pyrethrins + piperonyl butoxide 1:10.	373	
Musca domestica (")	Topical	LD$_{50}$ 24 hr	80.2 μg/g	Methoxy-I, R-strain; pyrethrins + piperonyl butoxide 1:10.	373	
Musca domestica (")	Topical	LD$_{50}$ 24 hr	62.5 μg/g	Lindane-I, R-strain; pyrethrins + piperonyl butoxide 1:10.	373	
Musca domestica (")	Topical	LD$_{50}$ 24 hr	89.9 μg/g	Multi-I, multi-R strain; pyrethrins + piperonyl butoxide 1:10.	373	

(2) Observations by various investigators (Continued):

Insect	Route	Dose	Dosage	Remarks	
Musca domestica (adult)	Topical	LD_{50} 24 hr	56.8 μg/g	Lab-I, non-R strain; pyrethrins + piperonyl butoxide 1:10.	373
Musca domestica (")	Topical	LD_{50} 24 hr	49.1 μg/g	Lab-II, non-R strain; pyrethrins + piperonyl butoxide 1:10.	373
Musca domestica (")	Topical	LD_{50} 24 hr	258.7 μg/g	Pyro-I*, pyrethrin-R strain; pyrethrins + piperonyl butoxide 1:10.	373
Musca domestica (")	Topical	LD_{50} 24 hr	81.6 μg/g	Multi-III, multi-R strain; pyrethrins + piperonyl butoxide 1:10.	373

*21 generations of selection by exposure of larvae and adults to pyrethrins; origin of strain: Lab I.

Chironomus spp. (larvae)	Medium	LC_{100} 90-93 hrs	12 ppm w/w	0.9% pyrethrins as pyrethrum powder.	979 Fellton,
Lygus atriflavus elisus hesperus (nymph)	Dust	LDeposit$_{50}$ca	25.9 mg/100cm^2	A dust $\bar{c}$ 2% pyrethrins and talc.	1010 Fisher and 19
Lygus " (adult)	Dust	LDeposit$_{50}$ca	>11 mg/100cm^2	"	1010
Lygus " (nymph)	Dust	LDeposit$_{100}$ca	>47.5 mg/100cm^2	"	1010
Lygus " (adult)	Dust	LDeposit$_{100}$ca	47.5 mg/100cm^2	"	1010
Lygus " (adult, nymph)	Dust	LDeposit$_{97}$	31.8 mg/100cm^2	Pyrethrum + cubé.	1010
Musca domestica (adult)	Topical	LD_{50} 24 hr	1.0 μg/fly	At 60°F; Lab strain DDT-non-R strain.	371 Bruce 19
Musca domestica (adult)	Topical	LD_{50} 24 hr	0.94 μg/fly	At 60°F; Bellflower, DDT-R strain.	371
Musca domestica (adult)	Topical	LD_{50} 24 hr	1.6 μg/fly	At 60°F; Pollard, DDT-R strain.	371
Musca domestica (adult)	Topical	LD_{50} 24 hr	1.13 μg/fly	Piperonyl butoxide-pyrethrins 10:1.	371
Aceratogallia sanguinolenta	Dipping	LC_{100}	ca. 2604 g/100cc H_2O	As a suspension; exposure 30 seconds.	3239 Watkins

d) Comparative toxicity of pyrethrins and other compounds for insects:

(1) Vs. Musca domestica; topical application by measured drop method: 78 Anon.,

Strain	LD_{50} (μg/fly) 24 Hrs For						
	Pyrethrins	DDT	DDD	Methoxychlor	Toxaphene®	Lindane	Heptachlor
Bellflower (DDT-R)	1	10	20	1	0.6	0.08	0.06
San José (")	2	0.7	-	0.3	0.4	0.05	0.07
Ontario (")	2	0.5	-	0.3	0.5	0.05	0.07
Riverside (")	2	0.5	-	0.3	0.5	0.06	0.07
Laboratory (DDT-non-R)	1	0.02	0.1	0.07	0.2	0.01	0.03

(2) Vs. Musca domestica and Aëdes aegypti adults by spraying with pyrethrins 0.1% w/v for Aëdes and 2.0% w/v for Musca; DDT and BHC . .3%; all in odorless distillate + benzene (50:50). 693 Davis 4

Insecticide	LD_{50} (μg/g) For			
	Musca		Aëdes	
	♂	♀	♂	♀
Pyrethrins	31.0 (30 - 35)	38.0	0.5 (0.5 - 1.0)	1.0 (1.0 - 1.5)
DDT	6.0 (5.5 - 7.0)	9.0(9.3-10.5)	5.5 (4.5 - 5.5)	8.0 (7.5 - 8.5)
BHC	2.0	3.0	3.0	3.5

(3) Vs. Musca domestica; as acetone + kerosene (1:1) sprays: 1164 Gersdorff 4

Insecticide	Mean Concentration For 50% Mortality (mg/cc) 24 Hrs	Relative Toxicity At LC_{50}
Pyrethrins (standard)	1.2 ± 0.14	0.43 ± 0.06
Hexaethyl tetraphosphate	0.52 ± 0.05	1.0 (STANDARD)
Tetraethyl pyrophosphate	0.095 ± 0.01	5.5 ± 0.7
Parathion	0.03 ± 0.003	17.0 ± 2.0

(4) Pyrethrins and allethrin vs. various insects; spraying tests, with insects held at 17° - 20°C after treatment; treated in Potter tower; aqueous sprays 0.1% lorol + 10% acetone: 935 Elliott et al

I = (±)-3-methyl-2-allyl-cyclopent-2-en-4-ol-1-one esterified with (+)-trans-chrysanthemum monocarboxylic acid (natural acid) = pyrethrin.

II = +, (±)-allylrethronyl (+)-trans-chrysanthemate.
III = +, (±)-allylrethronyl (±)-cis-trans chrysanthemate.

(a)

** Insect	LD$_{50}$% (w/v) I	LD$_{50}$% (w/v) II
Plutella maculipennis (larva, last instar)	0.00899;0.00346	0.00251;0.00241
Macrosiphum solanifolii (adult, apterous ♀♀)	.000541;.000704	.00272; .0092
Phaedon cochleariae (adult)	.000371;.000305	.000662;.002009
Oryzaephilus surinamensis (adult)	.00552;.00789	.0112;.02607

**Data of various experiments performed at different times.

(b) Data from insects all sprayed on the occasion of the same experiment: A = natural pyrethrins, B = ± -allylrethronyl (+)-trans-chrysanthemate, C = ± -allylrethronyl (±)-cis-trans-chrysanthemate.

Insect	LD$_{50}$% (w/v) A	B	C
Plutella maculipennis (larva)	0.005754	0.001415	0.003162
Macrosiphum solanifolii (adult, apterous ♀♀)	0.00034	0.00275	0.00589
Phaedon cochleariae (adult)	0.000324	0.000813	0.001662
Oryzaephilus surinamensis (adult)	0.00537	0.01122	0.01318

(c) Relative potencies:

	Vs. Plutella	Vs. Macrosiphum	Vs. Phaedon	Vs. Oryzaephilus
A	1000	1000	1000	1000
B	3980	123	399	479
C	1820	58	200	406

(5) Vs. Pediculus humanus corporis and Cimex lectularius; spraying tests, with toxicants in P31 oil, the solutions sprayed at 0.36 mg/cm^2, a rate at which the oil carrier is harmless; contact spraying: 413 Busvine, 4

Insecticide	Pediculus LC$_{50}$(%)	Cimex LC$_{50}$(%)	LD$_{50}$ Pediculus μg/insect	LD$_{50}$ Pediculus μg/g	LD$_{50}$ Cimex μg/insect	LD$_{50}$ Cimex μg/g
Pyrethrins	0.47	0.045	0.085	42	0.02	5
Pyrethrins + 2% isobutyl undecylenamide	0.038	0.026	0.007	3.5	0.012	3
Lindane	0.016	0.051	0.003	1.5	0.023	6
DDT	0.030	0.56	0.054	27.0	0.25	63
Lethane® 384	1.5	4.0	0.27	135	1.8	450
Lethane® special	2.4	12.5	-	-	-	-
Thanite®	3.2	75.0	-	-	-	-
Lauryl thiocyanate	6.0	19.5	-	-	-	-
Bis-ethyl xanthogen	6.2	75.0	-	-	-	-
Lethane® 60	8.1	32.0	-	-	-	-
Benzyl benzoate	21.0	75.0	-	-	-	-

(6) As contact toxicants for larvae of several insect species; contact sprays: 350 Brown, 47

Insecticide	Lethal Deposit$_{50}$ (μg/cm^2) For Choristoneura fumiferana	Heliothis ononis	Agrotis orthogonia
Pyrethrins	0.05	4.0	8.2
DDT	0.3	7.0	80.0
Lindane	1.9	23.0	5.5
Chlordane	140.0	Ineffective	18.0
DNOC	4.0	16.0	7.5
Nicotine	42.0	400.0	Ineffective

(7) Vs. various insect species: [Ref. 2219]

Insect	Route	Dosage ~~(μg/g)~~ mg/g To Yield Mortality (%) Indicated: Pyrethrins I, II 50%	100%	Lethane 384 50%	100%	Sodium arsenate 50%	100%	Derris Resins* 50%	100%	Nicotine 50%	100%
Anasa tristis	Topical	.007	.026	-	-	-	-	-	-	.35	1.25
"	Injection	.01	.025	-	-	.02	.04	.010	.025	.20	.35
Bombyx mori (larva)	Topical	-	<.0004	-	-	-	-	-	<.0007	.004	.008
"	Injection	-	-	-	-	-	-	-	-	.003	.007
Ceratomia catalpae (larva)	Topical	.002	.006	-	-	-	-	.002	.005	.10	.20
"	Injection	.004	.006	-	-	.02	.03	.004	.006	.08	.15
Oncopeltus fasciatus	Topical	.008	.028	0.40	0.75	-	-	.025	.06	.19	.45
"	Injection	-	-	-	-	-	-	-	-	-	-

(7) Vs. various insect species (Continued):

mg/g.

Insect	Route	Dosage (~~µg~~/g) To Yield Mortality (%) Indicated									
		Pyrethrins I, II		Lethane 384		Sodium arsenate		Derris Resins*		Nicotine	
		50%	100%	50%	100%	50%	100%	50%	100%	50%	100%
Periplaneta americana	Topical	.0065	.012	0.96	2.3	.25	1.30	-	-	.65	1.3
"	Injection	.006	.011	0.17	0.40	.045	.07	.007	.013	.1	.2
Popillia japonica	Topical	.04	.13	.80	1.70	.85	1.70	.025	.06	.65	1.0
"	Injection	.04	.11	.30	.09	.05	.10	.04	.11	.40	.90
Tenebrio molitor	Topical	.035	.1	.85	1.60	-	-	.019	.075	3.2	4.4
"	Injection	-	-	-	-	-	-	-	-	-	-

*For dosage as rotenone per se use 25% of the given value.

(8) Vs. Chaoborus astictopus (overwintering larvae): 768

Deonier & Lindq
'4

Insecticide	PPM	Mortality (%)
Pyrethrum (without wetting agent)	0.33	100
	0.2	99
	0.033	66
Pyrethrum (+ Na lauryl sulfate wetting agent)	0.2	100
	0.1	93
	0.033	63
	0.016	36
Derris (as rotenone)	1.0	98.3
	.5	97.5
Phenothiazine	0.33	100
1-Phenylbenzothiazole (in oil + CCl_4)	0.33	100
	0.2	66

e) Other toxicity tabulations:

(1) Relative susceptibility of diverse insects to pyrethrum sprays (in Turkey Red Oil) and dusts (in talc); pyrethrum deposits at 0.38 µg/cm²: 2393

O'Brien & Spenser '

Insect	Spray % Mortality	Dust % Mortality
Bombyx mori	100	100
Agelastica alni	100	100
Vanessa polychloros	100	100
Euproctis chrysorrhoea	100	--
Athalia spinarum	100	--
Dendrolimus pini	100	96
Vanessa io	100	90
Vanessa urticae	100	--
Smerinthus ocellata	100	--
Agrotis spp.	5	10
Lymantria monacha	0	--
Stilpnotia salicis	0	0
Carpocapsa pomonella	0	0
Oryctes nasicornis	0	--
Melolontha spp.	0	--
Myzus persicae	0	--

(2) Stage of development and susceptibility to pyrethrin sprays; larvae of Stilpnotia salicis: 1822 Klinger, '36

Instar	% Mortality	Time For Death
I	100	12 hrs.
II	100	16 hrs.
III	100	3 days
IV	65	4 days
V	15	5 days
VI	5	5 days

(3) Pyrethrins and other compounds vs. Musca domestica (adult), Fannia canicularis (3 day laboratory reared adults; av. wgt. ♂ = 6.89 mg; ♀ = 7.35 mg). 1981

Lewallen '54

Insecticide	Approximate LD_{50} 24 Hrs (µg/insect)		
	Musca domestica ♀	Fannia canicularis	
		♀	♂
Pyrethrins	1.0	0.24	0.44
DDT	0.033	2.80	1.30
Methoxychlor	0.068	0.14	0.12
Lindane	0.01	0.76	0.39

(3) Pyrethrins and other compounds vs. Musca domestica (adult), Fannia canicularis (3 day laboratory reared adults; av. wgt. ♂ = 6.89 mg; ♀ = 7.35 mg) (Continued):

Insecticide	Approximate LD₅₀ 24 Hrs (µg/insect)		
	Musca domestica ♀	Fannia canicularis	
		♀	♂
Dieldrin	0.031	0.003	0.0026
Malathion	0.56	0.1	0.06
Diazinon	0.092	0.098	0.054
Chlorthion®	0.33	0.035	0.022

(4) Pyrethrins and chlorinated hydrocarbons as space sprays vs. Musca domestica (adult), applied by Campbell Turntable Method; sprays made up in kerosene; variations reflecting differences in resistance and susceptibility of various fly "populations": 1152 Gersdorff '

Insecticide	Concentration (mg/cc)	"KD" 25 min (%)	Mean Mortality 24 Hrs.	LC₅₀ (mg/cc)	Relative Toxicity Compared To Pyrethrins	Relative Toxicity Compared To Chlordane (tech)
Pyrethrins	8.0	100	82	3.32 ± 0.25; 2.83 ± 0.36 1.37 ± 0.16	1.0	-
	4.0	100	58;63			
	2.0	100	71;36;26			
	1.0	100	32;17;13			
Aldrin	0.25	7;5	85;82	0.131 ± 0.01 0.129 ± 0.017	25;22	4.0
	0.125	8;6	45;51			
	0.063	9;3	15;15			
Chlordane (tech) Sample A	1.0	8;10	99;84	0.33 ± 0.04 0.52 ± 0.039	4.2;6.4	1.0
	0.5	7;3	74;51			
	0.25	11;6	33;12			
Chlordane (tech) Sample B	1.0	9	93	0.39 ± .05	3.5	-
	0.5	11	70			
	0.25	6	20			
Chlordane (crystaline)	1.0	9	66	0.743 ± 0.055	4.5	0.7
	0.5	9	28			
	0.25	6	11			
Dieldrin	0.25	5	98	0.088 ± 0.011	32	5.9
	0.125	1	74			
	0.063	2	27			
Heptachlor	0.5	14;-	100 -	0.114 ± 0.009	ca 28	4.0;4.4 (73% Mortality Level)
	0.25	8;4	100 93			
	0.125	7;5	73 45			
	0.063	- 7	— 17			

(5) Susceptibility of Periplaneta americana and Blattella germanica to pyrethrin sprays, directly applied to dorsum; concentration = 5 mg pyrethrins per cc kerosene: 2177 McGovern '

Stage	Spray Deposit (µg/cm²)	% Mortality Of Periplaneta	% Mortality Of Blattella
Adult ♀	960	--	100
" "	560	100	72
" "	280	56	27
Large Nymphs	960	--	87
"	560	77	60
"	280	52	25

"KD" more rapid for Periplaneta; Blattella more resistant to killing effect.

Pyrethrum (0.9% pyrethrins) as a dust at 0.81 mg/cm² for Blattella germanica, topical application gave 14% mortality in 24 hours; 100% mortality in 96 hours; average survival time ♂ = 7.8 hours, ♀ = 49.3 hours. Pyrethrum 25% + pyrophyllite 75% topical application gave 81% kill in 24 hours, 86% kill in 96 hours; average survival time ♂ = 3.5 hours, ♀ = 26.6 hours. 777 Dewey '42

(6) Relative susceptibility of Stomoxys calcitrans and Musca domestica to pyrethrum and kerosene sprays; used as OCI (Official Control Insecticide of the National Ass'n. of Insecticide and Disinfectant Manufacturers) as a mist, in vault (28.5 m³) at 27°C; exposure 10 minutes: 887 Eagleson '

Insect	Dose (cc. OCI)	Fraction of LC₅₀ For Musca domestica	Result
Stomoxys calcitrans	5.6	1/10	100% initial torpor; 100% kill.
"	2.8	1/20	" " " ; " " .
"	1.12	1/50	97% " " ; " " .
"	.56	1/100	<75% " " ; 93% " .
"	.56 + 9.4 cc refined kerosene	1/100	<75% " " ; 88% " .
"	5.6cc refined kerosene	--	10% disabled
Musca domestica	55.90	1/1	98% initial torpor; 51% kill.

(7) Vs. Aceratogallia sanguinolenta; pyrethrum as a powder (0.92% total pyrethrins); by immersion for 30 seconds in water-suspension; dosage and net mortality %: 3239 Walkins,'42

g/100 cc H_2O	Net Mortality %
1.0416	100
.521	100
.2604	100*
.1302	98.9
.0651	89.3
.0326	65.8
.0163	43.2
.0082	22.0
.0041	17.7
.0021	3.5

(* = to 4 lbs. of 0.5% flowers/100 gal.)

(8) Effect on Phormia regina dipped in (A) = solutions of a commercial insecticide: Esters of mannitan + coconut oil fatty acids + pyrethrins 1% and (B) = control using foregoing esters without pyrethrins; insects of various ages: 70 Anderson & Hank,'4

(Age of flies →)	3 - 12 hrs		<5 minutes	36 - 48 Hrs	<5 minutes
Material dilution	% Kill 48 Hrs. After Dipping for 15 Seconds in				
	A	B	A	A	A
1:100	100	83	--	--	--
1:200	100	100	--	--	--
1:400	100	67	--	100	33
1:800	100	33	10	89	11
1:1600	100	50	10	89	11
1:3200	88	17	0	33	0
1:6400	33	0	0	0	11
1:12,800	14	17	0	--	--
1:25,600	14	17	--	--	--

(9) Effects of atmospheric environment (temperature, relative humidity) before and after treatment; adult Tribolium castaneum sprayed with pyrethrins in aqueous medium, with or without terpineol; hot = 80°F, cold = 60°F; at 80° relative humidity = 60%; at 60° R. H. = 48 - 56%: 2532 Potter & Gillham '4

Treatment of Insects		Terpineol	LD_{50} As % Total Pyrethrins (w/v)	
Before Spraying	After Spraying	(present (+) absent (-))	Experiment I	Experiment II
Cold	Cold	(-)	0.0044	0.0031
Hot	Cold	(-)	.0049	.0033
Cold	Hot	(-)	.0092	.0098
Hot	Hot	(-)	.0116	.0156
Cold	Cold	(+)	.0027	.0018
Hot	Cold	(+)	.0045	.0018
Cold	Hot	(+)	.0122	.0110
Hot	Hot	(+)	.0198	.0125

Insecticide	Medium	Potency Under Cold Storage (As Proportion Of Potency Under Hot Storage)		
		Cold Before Spraying	Cold After Spraying	Cold Before, Cold After
Pyrethrins	aqueous	1.19;1.31	2.25;3.84	2.67;5.01
Pyrethrins + terpineol	"	1.62;1.07	4.45;6.49	7.21;6.9
Lauryl thiocyanate	"	0.98	1.47	1.43
Nicotine	"	0.99	1.24	1.23
DNOC	ethylene glycol	--	--	1.46
DDT	Wakefield oil	--	--	2.61
Wakefield half-white oil		--	--	0.87

f) Toxicity for beneficial insects: (Also see Bees and Insecticides)

(1) Safe for Apis mellifera within a few minutes of application. 3099 Todd,'49

(2) As a spray of pyrethrum with 6% extractives, at 1 part to 400 parts water, the average kill of Hippodamia convergens larvae (1st instar) = 8% (3 - 13%); of eggs = 3% (0 - 9%). 1450 Haug and Peterson,'38

g) Pharmacological, pharmacodynamic, physiological, etc.; for insects:

(1) Mode of action:

(a) Primarily contact insecticides; modest stomach toxicity. 2231,353,2815 Shepherd 51

Metcalf,'55, Brown,'51

(b) Manifestations following oral intake; various insects: 1059,757,2120

Insect	Sequelae Of Oral Intake	
Agrotis segetum	Regurgitation, spasm, quiescence → recovery.	3207
Pieris brassicae	" " .	3207
Porthetria dispar	" " .	3207
Locusta migratoria migratorioides	" " .	3207
Blatta orientalis	Symptoms disappearing after 12 hours.	1545
Prodenia eridania	No effects following oral intake; susceptible to contact action.	3348
Apis mellifera	Highly toxic on oral intake.	296
Mosquito larvae	Little or no pyrethrins in tissue, digestive tract or feces 6 - 24 hrs. after intake.	353

(c) Manifestations of contact action:

	Sequelae Of Contact Exposure	
Tenebrio molitor Periplaneta americana	Applied as droplets 0.15% pyrethrins in kerosene to antennae, cerci, legs, head, spiracles abdomen, thorax: Gave toxic symptoms arising after application to neck and intersegmental areas in ½ the time required after application on highly sclerotized areas.	2405
Macrodactylus subspinosus	— 1 drop pyrethrin on tarsus brought rapid death.	1429
Glossina morsitans	— Application to pulvilli gave paralysis in 2 seconds or more.	2535
Blatta orientalis	— Topical application as 25% pyrethrum dust: For 1.5 minutes no reaction; after 2 minutes sudden, intense excitement then paralysis first of the metathoracic legs followed by spread of paralysis to other members rendering the insect helpless in 8 minutes. Effects localized on restricted local application; ½ or more of surface must be dusted to ensure total paralysis in 12 hours. Application directly to tracheae proved ineffective.	1545
Periplaneta americana	Applied as dry powder in spiracles: Brought symptoms (legs) similar to those noted after giving kerosene solutions of pyrethrins by injection.	2713

(d) Rate of penetration * (measured as approximate time for paralysis) of pyrethrins in various solvents through the cuticle of Rhodnius prolixus after topical application; 2% solutions of pyrethrins: 3297

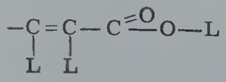
Solvent	B.P. (°C)	Time For Paralysis To Occur
Hexane	-	1.25 hrs.
Heptane	-	1.5 hrs.
White Spirit	150-190	2 hrs.
White Oil	265-365	5 hrs.
White Oil	310-390	10 hrs.
Odorless Distillate	200-260	4 hrs.
A 12 Oil	260-360	6 hrs.
P 31 (refined heavy paraffin oil)	320	6-28 hrs.
Oleic acid	-	4.5 hrs.
Olive Oil	-	36-96 hrs.
Castor Oil	-	36-96 hrs.
Sesame Oil	-	36-96 hrs.

*Onset of symptoms correlated with boiling point of solvent; vegetable oil solvents yield slow response; pretreatment with petroleum ether speeds the onset of symptoms. Response also associated with cuticular thickness: At 8 - 9 micra cuticle thickness 1.5 hrs; at 10 micra 2 hrs; at 18 micra 8 hours.

(e) Musca domestica and Aëdes aegypti flying through finely dispersed pyrethrin mists (sprays in odorless kerosene + benzene [50:50]) accumulate a large proportion of the dose on the wings. Addition of Sudan III shows penetration of wings directly, with later appearance in Malpighian tubules; the material may also be removed from wings in the grooming process and be transferred to and absorbed via the legs. 693

(2) Theories of toxic action of pyrethrins: 934

(a) By some the toxophoric portion of the pyrethrin molecule is thought to be at 1933



$-\underset{\underset{L}{|}}{C}=\underset{\underset{L}{|}}{C}-C\overset{=O}{-}O-L$

where L = a lipid solubilizing group; the cyclopropane ring, methyl, dimethyl and allene groups are believed responsible for lipid solubility.

(b) Another theory is based on cuticular permeability to pyrethrins with subsequent effects on tissue receptors controlling oxidative enzyme systems. Access of pyrethrins to insect interior facilitated (a postulate) by absorption and storage in epicuticular lipophilic layers. According to this theory, "pyrethrinization" consists of: I) Narcosis ("knockdown") phase, with block of oxidase action by absorption of pyrethrin to lipo-protein tissue complexes; II) death follows when a dispersant action brings on irreversible increase in phenol oxidase activity (through displacement of protective lipids) which leads to build-up of toxic metabolites in blood and tissues. Relative susceptibility and refractoriness of various insect species is laid to differences in cuticle make-up and internal factors associated with oxidase system stability. 1629 1627

(3) Age of insects and sensitivity to pyrethrins: (See some of the preceding tabulations in the part headed Toxicological).

(a) In the case of the tick Ornithodorus moubata (Argasidae) older larvae react more slowly to immersion in pyrethrin solutions than do young larvae. 2679

(b) Young Musca domestica adults are more rapidly paralyzed and less rapidly killed by sprays than older subjects. 2837, 70

(c) Vs. Loxostege sticticalis larvae pyrethrin dusts and sprays proved very effective in case of instars I, II, III; practically ineffective for instar V (there is a decrease of fat in the exoskeleton from 11.7% in instar III to 0.2% in instar V). 2471

(4) Site of application and "knockdown" effect:

(a) Application of 1 μg pyrethrins in kerosene to the thoracic dorsum of Musca domestica, Calliphora vomitoria gave 40% "knockdown" (on the average) in 13 minutes; application to mouth parts and thoracic spiracles gave 100% "knockdown" in 1 - 3 minutes; application of 0.01 μg in kerosene at the cervical membrane and inter-coxal regions gave instantaneous "knockdown". 3318

(5) Miscellaneous factors influencing penetration of the insect body by pyrethrins:

(a) Increase in relative humidity enhances penetration and hastens onset of symptoms in Lymantria monacha (larva) treated at 21°C with pyrethrum dusts. 329

(b) Solvents with high surface activity, such as alcohols, aldehydes, ethers and esters penetrate rapidly the cuticle cut from living insects; disaccharides and amino-acids (with little surface activity) penetrate not at all or slightly; fatty acids and paraffins do not enter. 329

(c) Mixtures of polar and apolar solvents (alcohol and paraffin oil) penetrate the cuticle of Calliphora erythrocephala (larva) with extreme rapidity (4 - 6 minutes) while neither one alone is effective within 1 hour. 1626

(d) Reported by some that the partition coefficient of a toxic material, such as pyrethrins, determines the rate at which it will leave an oily carrier to enter the insect cuticle. 3299

(6) General toxic effects of pyrethrins; symptoms, signs:

(a) Symptom sequence which followed the placing of a droplet on the dorsum of Protoparce sexta (larva): Insect normal for ½ hour; last pair prolegs affected; paralysis of treated segment; regurgitation; insect rolled over and over for ca. 15 minutes; uncoordinated, violent movements for ca. 30 minutes; locomotion ceased; death in ca. 24 hours. A droplet on head: Beginning of response in 8 minutes. Injection into last abdominal segment: Intoxication in 2 minutes. 1429

(b) Rhodnius prolixus: Pyrethrin treatment leads to: I) incoordination of hind legs; II) all legs uncoordinated but walking possible; III) inability to walk, progressive extension of proboscis; IV) paralysis, which may continue 10 - 20 days, with the heart beating and continued gut movements. 3297

(c) Blattella germanica pyrethrin treated (oil solutions) showed: At ca. 2 second latent period; (dusts) 5.5 second latent period followed by intense excitement then submaximal activity with legs incompletely relaxed. 1632

(d) Thermobia domestica, recovering from sub-lethal pyrethrin exposure, reveals delayed effects: Appearance of discolored areas, sloughing of appendages, (legs, antennae, cerci, palpi, ovipositor) appearing as long as 19 weeks following exposure. 353

(7) Physiological action of pyrethrins:

(a) Effects on heart rate: in Corethra larvae: Progressively slowed. 1865
in Galleria mellonella: Slowed; diastole prolonged. 213
in Blatta orientalis: Heart stopped in systole. 3382
in Bombyx mori: Applied to heart at 0.007% in saline: Amplitude and frequency increased; at 0.01% in saline: Amplitude and frequency decreased followed by frequent and partly reversible cessation of beat. 1598
In the pyrethrinized Rhodnius heart beat may continue 10 - 20 days after complete paralysis. 3297

(8) Locus of action:

(a) Primary action is most probably on the central nervous system, with apparent blocking of nerve impulse transmission. Histopathological changes occur in the neurons. The evidence supporting this conclusion: I) A stimulating effect leading to paralysis and death; II) histopathological changes; III) accumulation and threshold concentration prior to action; IV) early loss of nerve responsiveness to electrical stimulation; V) selective penetration to nervous system; VI) effects on the action potential. 151,2713, 3278,1865, 777,1420, 2047,2600, 893

(b) In Periplaneta americana: 1632,2713

Application of pyrethrins to abdomen (nerve cord sectioned at 3rd abdominal segment): On legs no effect; abdominal twitching.

Applied to thorax: Twitches in the isolated legs.

Isolation of abdomen behind 3rd segment save for nerve cord: No prevention of pyrethrin action.

Applied to abdomen (nerve cord sectioned): Death.

Applied to cut end of isolated leg: Muscle fibrillation, slow contraction.

Applied to thoracic ganglion: Immediate paralysis of legs innervated thereby.

Applied to abdomen (nerve cord severed in ganglion): Leg paralysis posterior to the site of section.

Applied to leg: Stimulation of crural nerve yielded discharges at ever shorter intervals with contraction of leg followed by continuous action potential discharge volleys. 520

Applied to nerve, in nerve-muscle preparations: 0.01 - 0.1 ppm were active on neuraxon yielding rhythmic, spontaneous discharge at a potential lower than with DDT; 1 ppm gave rapid action on nerve trunks with spontaneous discharge in 1 minute; at more than 1 ppm caused blockage of nerve conduction, the effect being reversible by prolonged washing. 3278

- (c) In Blatta orientalis:
  Application to nerve cord yielded massive discharge followed by repetitive, synchronized, discharge of nerve impulses, then gradual decline to failure of all response. 2047
- (d) Claimed by some that pyrethrins act on peripheral nerve system of insects at a site only a few thousands of a mm from the external surface. 2432

(9) "Pyrethrinization" and histopathology:

- (a) Applied to Periplaneta as a concentrate via the 1st thoracic spiracle: I) Immediate initial paralysis; II) partial recovery in a few minutes; III) gradual decline with slower and slower peripheral movements; death. Movement of legs, heart and abdomen may continue more than 50 hours; $\frac{1}{2}$ - 52 hours after treatment no response followed electrical stimulation of the nerve cord. 2600
- (b) Tissue effects after the preceding treatment: 2600
  Analysis of nerve tissue in polarized light: Affected first the axoplasm then the lipid component of the nerve sheath where the most prominent lesions appeared. The birefringent ultrastructure was disorganized and lost prior to cessation of movement, but not prior to central nerve cord paralysis. The fine structure degeneration was progressive with time, extending from the region of maximum penetration and spreading. The action was selective on nerve tissue with degeneration of the axoplasmic colloids and of the nerve cell body plus later sheath degeneration and vacuolization. Normal post-mortem effects which followed death of the nerves from pyrethrum treatment complicated the histological analysis qua specific pyrethrum effect.
- (c) Vacuolization of ganglia and nerve cord appeared in 10 - 20 minutes after the onset of convulsions in Corethra, the phenomenon being absent in larvae convulsed by sublethal doses. 1865
- (d) In Melanoplus femur-rubrum and Tenebrio molitor (larva) lesions of brain, ganglia and connectives, were present 16 hours after external application of pyrethrins; vacuolization and disintegration of the involved nerve tissue was present and death was attributable to neuron destruction. Neuropathology is also described from Rhodnius, Cimex, etc. after pyrethrum treatments. 1420 1422 2600 3297

(10) Biochemical effects:

- (a) In vitro preparations of Periplaneta americana coxal muscle cytochrome oxidase were completely inhibited (as measured by O_2 uptake in Warburg's apparatus) by pyrethrins and allethrin, at 10^{-5} M concentrations. 2305

(11) Metabolic:

- (a) The reversible nature of pyrethrin paralysis suggests possible detoxification. Hydrolytic enzymes (such as esterases) attacking pyrethrins to produce non-toxic metabolites have been postulated. 6
- (b) Prodenia eridania is reported to detoxify orally administered pyrethrins in 6 - 12 hours. 3348
- (c) Incubated with blood, fat body, skin, muscle and intestine homogenates of Prodenia, pyrethrins were decomposed to various degrees, the fat body being most efficient in the breakdown. 3348
- (d) Periplaneta - derived lipase hydrolyzed pyrethrins. 508
- (e) Other metabolic mechanisms have been brought forward in Refs. 3336, 3397, 3333.

h) Temperature and the insecticidal action of pyrethrins:

- (1) A negative temperature coefficient has been reported for pyrethrum in its action vs. Circulifer (= Euttettix) tenellus, Musca domestica, Blattella germanica, Macrodactylus subspinosus and Apis mellifera, with increased activity of the toxicant being noted at lower temperatures. 273
- (2) Temperature and the action of pyrethrum vs. Periplaneta americana; C^{14} labelled (radioactive) pyrethrum in topical application: 273
  - (a) Topical LD_{50} (24 hrs) = ca. 1 μg/insect at 15°C or ca. 6 μg/insect at 35°C.
  - (b) At 35°C the rate of pyrethrum penetration into the interior of Periplaneta was more than twice that at 15°C.
  - (c) Insects, prostrate at 15°C from pyrethrum poisoning, may be returned to normal by transfer to an environment at 35°C; the process may be repeated over a period of several hours.
  - (d) Since pyrethrum treated Periplaneta, transferred from 35°C to 15°C become prostrate faster than those continuously held at 15°C, it is assumed that the insecticide (or some metabolic "toxin") was present in the vicinity of the action site at 35°C, but remained ineffective at that temperature.
  - (e) Pyrethrum poisoning in Periplaneta is stated to be associated with the presence of a haemolymph-borne "toxin" which does not show its toxicity at 35°C.
  - (f) Using C^{14} labelled pyrethrum it was shown that haemolymph from pyrethrum-treated roaches was not radioactive, indicating that a material in the blood and toxic to the insect is not pyrethrum.
  - (g) Bioassay of the blood of pyrethrum-treated Periplaneta using adult Sarcophaga crassipalpus indicated that symptoms of poisoning in the roach were correlated with the "toxin" content of the haemolymph.
  - (h) Piperonyl butoxide enhanced the susceptibility to pyrethrum of Periplaneta at higher temperatures.
  - (i) The "toxic principle" in the haemolymph of pyrethrum-treated Periplaneta lost its activity when stored at room temperature.

i) Synergism; pyrethrins and other compounds: (Also consult, Synergism General Treatment and individual synergistic compounds): 1755,353 2231,3037,2432

- (1) Pyrethrum represents par excellence the insecticide for which synergistic action is both most clear-cut and well known.
  - (a) The temporary paralytic effect of small dosages of pyrethrins ("knockdown") and the lethal effects of larger doses are potentiated by from 2 to 12 times when pyrethrins are applied with certain synergistic substances, such as N-isobutyl undecylenamide, piperonyl butoxide, piperonyl cyclonene, n-propyl isome, ethylene glycol ether of pinene, N-(2-ethylhexyl)-bicyclo [2,2,1] -5 heptene-2, 3-dicarboximide, sesamin, etc., substances in themselves of very modest or no insecticidal power.

(b) The effect is one of true potentiation, the synergist (itself non-toxic or nearly so) permitting the use of quantities of pyrethrin much smaller than would be required to bring about a given toxic effect with pyrethrins alone. The synergistic effect abides when all considerations of droplet size, stabilization of insecticide and other physical effects are ruled out. 2432

(c) With sesamin and N-isobutyl undecylenamide the toxicity of pyrethrins is raised by a factor of 3 when up to equimolecular proportions of the stated substances are present; further increase of synergist brings in increased effect. Example: Vs. Aëdes aegypti the addition of synergist decreased the mean weight of pyrethrins needed to paralyze each insect from 6.0 to 2.0 x 10^{-7} mg. Once a 1:1 molecular ratio of pyrethrin + synergist was achieved no further fall in "knockdown" threshold quantity of pyrethrins was possible. There is postulated a complex (3 times as toxic as pyrethrins alone) acting at the peripheral nerve sheath interfaces and so reorientating the pyrethrin molecules that a more efficient discharge of resting potential at the interface occurs. 2432

(d) The sharp limitation of synergistic action when pyrethrin + synergist reach equimolecular proportions (noted with flying Aëdes) was confirmed for Sitophilus granarius crawling on deposits of pyrethrins (as oil films) from oil solution. Piperonyl butoxide seems exempt from the equimolecular limitation. 249

(e) Using pyrethrins and piperonyl butoxide or N-isobutyl undecylenamide as synergists vs. Musca domestica and Cimex lectularius the toxicity of pyrethrins was increasingly potentiated with a rise in ratio of synergist + pyrethins to at least 20:1; enhancement was greatest for the lower ratios for instance, falling off with further increase of ratio. 2344

(f) Piperonyl butoxide appears to be the most powerful synergist of pyrethrins, increasing pyrethrin potency vs. Musca by 5 times (allethrin by 4 times) and vs. Cimex by 2 times (allethrin by 3 times.) Isobutyl undecylenamide enhanced the potency of pyrethrins (+ allethrin) by no more than twice for either Musca or Cimex, using the measured drop or residual film methods. Piperonyl butoxide greatly prolonged the effectiveness of pyrethrin residual films. 2344

(g) Synergism (by independent joint action) is reported for pyrethrins and nicotine for Tribolium confusum in dipping tests. The maximum synergism observed was 2-fold. Application of nicotine, followed by pyrethrins at intervals of 0.75 to 6 hrs showed the greatest toxicity at the shortest interval; evidence of synergism became virtually nil with intervals of more than 6 hours. 3139

(h) A standard concentration of 2% piperonyl butoxide with 0.2% pyrethrins (formulated as water miscible emulsions completely free of mineral oils or objectionable ingredients) may be directly applied to grain in storage to control insects. Using 2-12 gallons of emulsion per 1000 bushels grain, protection was conferred for many months. 833

REPELLENCY OF PYRETHRINS FOR INSECTS:

1) Diataraxia oleracea (larva, final instar) is reported to be violently repelled on biting the leaf of a host plant treated with extract of natural pyrethrum. 3245

155

REPELLENTS

1) Action of certain repellent substances, deemed safe for man, on various mosquitoes; evaluated as average repellent time (time from application of the repellent to the recording of the first bite) in minutes. 3116

Repellent					Average Repellent Time (Minutes) As Mixture* For	
	Aëdes aegypti	Aëdes (sp) (Alaskan)	Aëdes taeniorhynchus	Anopheles quadrimaculatus	A. aegypti	Aëdes sp. (Alaskan)
Acetoacetic acid, cyclohexyl ester	109	21	102	57	232	61
Bicyclo (2,2,1)-heptene-2,3-dicarboxylic acid, dimethyl ester, cis-dimethyl carbate	229	85	208	48	305	95
Cinnamic acid, propyl ester	173	-	237	74	263	32
1,2-Cyclohexane dicarboxylic acid, diethyl ester	176	-	96	57	344	-
Ethanol, 2-phenoxy-, acetate	166	46	100	53	261	49
Ethanol, 2,2′-thiodi-, diacetate	237	20	57	47	244	29
2-Ethyl-1,3-hexanediol	331	21	283	53	271	57
Hydracrylic acid, β-phenyl-, ethyl ester	262	6	83	42	169	15
Dimethyl phthalate	247	19	155	108	-	-
Phthalimide, N-sec.-butyl	201	11	77	55	274	62
Propionic acid, diester with 1,5-pentanediol	160	10	95	93	203	43
Indalone®	111	9	168	41	-	-
Succinamic acid, N,N'-dipropyl-, ethyl ester	322	101	182	61	203	68
Tartaric acid, diisopropyl ester	255	3	74	40	290	18

* Mixture: 6 parts dimethyl phthatate, 2 parts Indalone® and 2 parts of the compound listed in the first column of the table.

156

RESISTANCE (A consideration in general terms of the so-called acquired resistance of insects to insecticides)

GENERAL CONSIDERATIONS

[Refs.: 2233, 3269, 2213, 2559, 148, 154, 353, 2723, 2274, 374, 372, 1805, 2021, 2097, 2558, 2972, 230, 282, 438, 763, 765, 972, 1091, 2052, 1803, 1761, 1597, 433, 2110, 103, 2256, 2223, 1193, 2376, 423, 1762, 2434, 1012, 78, 3320, 1260, 3269, 3057, 2474, 1259, 2971, 431]

More than 40 years ago it was noted that from "populations" of insects, once susceptible to particular toxicants at a certain level, resistant biotypes or strains had appeared which were tolerant of the formerly controlling toxicant concentrations. Among the early observations of tolerance (arising seemingly de novo) were those concerned with hydrogen cyanide-tolerant biotypes of Aonidiella aurantii, lime-sulfur-tolerant Aspidiotus perniciosus and the tolerance toward lead arsenate, phenothiazine and tartar emetic of other insects. In all instances, tolerance appeared among insects exposed by field treatment over a period of time with the agent of which they had become tolerant.

Recently, attention has dwelt on resistant insect biotypes which have been noted following field or laboratory exposures to DDT, chlordane, lindane, methoxychlor and other modern halogenated hydrocarbons. New interest now arises because of the tolerance observed among insects for some of the phosphoric acid and related esters which are attaining prominence in insect control. Of special interest, and consequently particularly studied, have been the insecticide-tolerant biotypes or strains of Musca domestica and species of the genera Culex, Aëdes, Anopheles, Pediculus, Blattella and Periplaneta.

DEFINITIONS

[Refs.: 2223, 1762, 3057, 373, 1326, 915, 1465, 1171, 1765, 103, 332, 1201, 2256, 72, 1363, 1440, 2169, 2198]

1) Operationally, the insecticide tolerance or resistance here considered is that which may be observed in the laboratory when an insect colony, for instance, Musca, Drosophila, Culex or Aëdes is exposed to a toxicant at a dosage which allows survival of some few individuals, and the continued exposure of the survivors and their progeny through as many generations as are necessary to raise the "developing" tolerance to its highest level.

   a) Exposure of an insect "population" in the field over a period of time may effectively accomplish the same result. In this case individuals which survive continuous or repeated exposure to an insecticide renew the "population". If the initial tolerance is due to something more than a casual or circumstantial factor, a biotype showing enhanced resistance to the toxic agent may soon appear. Against such a tolerant biotype heavier applications of insecticide may be made, thus increasing the selection pressure and permitting only the more tolerant to survive. At last, through continuous exposure, a maximally tolerant biotype occupies the field as a more or less fixed breeding group. Against this biotype the given insecticide of which it has "become" tolerant may be ineffective at dosages practically, economically or safely applicable. Such a course has been observed in the case of the rapid increase of tolerance for DDT on the part of Musca in a few seasons on dairy farms where fly-breeding places and harborages of adult flies were regularly DDT-treated.

   b) To this type of tolerance the loose designation of "acquired-" or "developed"-resistance has been applied. Various interpretations have been offered to explain these observations.

ORIGIN, NATURE, COURSE OF DEVELOPMENT AND INTERPRETATIONS OF INSECTICIDE RESISTANCE

1) Resistance to DDT on the part of Musca domestica, Drosophila spp. and mosquitoes is chosen because 2723,2274
it provides the best-authenticated laboratory and field examples. From these examples generally 374,372,1805
applicable observations emerge. 2021,2097,2558,2972

   a) Resistance to DDT has appeared among housefly "populations" in many places and has been 2223,230,282,438
   experimentally elicited from laboratory strains (or colonies) by the exposure to DDT of suc- 763,765,972,1091
   cessive generations arising from an initially DDT susceptible "population." 1803,2052,373

      (1) Best results are obtained by exposure of the whole life cycle of any insect to DDT especially the adult and larval stages. Exposure to DDT at a dosage which allows survival of some few individuals eliminates susceptibles and selects tolerants for survival, this being followed by inbreeding of the tolerant survivors. Intensive selection of adults and larvae by exposure and inbreeding of the survivors leads to "fixation" of biotypes with at least some degree of tolerance. 373

      (2) Tolerance establishment is comparatively slow during the first several exposed generations. Resistance does not develop at the same rate for all toxicants, even under intense selection. 373,736

      (3) Once distinct tolerance or resistance is manifested, a rapid increase and intensification to the maximum tolerance by increasing selection pressure is possible and easy. Pressure of repeated exposure raises tolerance to such levels that certain biotypes of Musca can be constantly maintained in heavily DDT-treated environments. 373

(4) With continued inbreeding, *Musca* biotypes tolerant of DDT have retained a constant level of tolerance 373
in absence of further DDT-exposure for more than 30 generations. The ultimate level of tolerance
attained may greatly vary, depending apparently on the nature of the original "population."

(5) DDT-tolerant *Musca* biotypes, whether of field or laboratory origin, are often comparatively tolerant 373,1831
of DDT-analogues or DDT-like compounds.

(6) Biotypes tolerant of DDT "acquire" tolerance of (or resistance to) other insecticides such as chlordane, 373
dieldrin or lindane, following suitable exposure, in less time than was required by the biotype to attain 2231
DDT-tolerance, or in less time than is needed by a generally susceptible "wild-type" strain. For ex- 2095
ample, the DDT-R *Musca* biotype "Pollard" showed lindane resistance after 3 exposures. Certain field
strains resistant to DDT showed lindane and dieldrin tolerance after 2 seasons of exposure and simul-
taneously achieved enhanced DDT-tolerance. DDT-R "Pollard" after 3 lindane exposures became
simultaneously relatively resistant to most chlorinated hydrocarbon insecticides. Also, exposure of a
strain resistant to methoxychlor ("Methoxy-I") to a chlorinated hydrocarbon mixture yielded a biotype
moderately resistant to most tested materials. This phenomenon constitutes "cross tolerance."

(7) The genetic factors responsible for DDT-tolerance are borne by both ♂ and ♀ *Musca*, are not sex- 373,684
linked and the inheritance of tolerance is on a multiple gene basis constituting an example of multiple 1411
factor inheritance with many genes and modifiers being in interaction in the resistant genotype. 2389,2512

(8) Certain DDT-tolerant biotypes have shown in the field no loss of resistance after 2 years discontinu- 2231
ance of DDT use. Laboratory tolerant biotypes have retained resistance through 30 to 50 generations 658
at a high level. However, in some instances reversion to susceptibility has been noted. 2512

(9) Increased tolerance of DDT by mosquitoes has been recorded in various parts of the world. The tol- 2231
erance has been transmitted, in absence of further exposure, through at least 8 generations. Larvae
have shown the same tolerance as their tolerant adult parents.

(10) DDT-tolerance has been shown to be accompanied, in some well-studied biotypes, by the ability to 2474
metabolize DDT by enzymatic dehydrochlorination, more or less rapidly or completely, to non-toxic 2971
or less toxic substances.

(11) Developmental rate, size and behavior in some DDT-tolerant biotypes may differ from those of various 2231
DDT-susceptible "populations."

(12) Crosses between DDT-tolerant biotypes characterized by markedly different levels of resistance yield 373
hybrids which are "physiological blends" in their tolerance of DDT (blending inheritance) being inter- 2263
mediate between their parent strains in tolerance. Such "blends" are reported to have persisted
through 15 generations of inbreeding without change and in absence of added selection by further DDT
exposure.

2) *Interpretations*: [Refs.: 2223, 423, 1412, 2477, 1597]

a) Two general premises are available for interpretation of insecticide tolerance:

I) Natural selection (the toxicant being an agent of this) acting upon the available genetic variability in a 2223
heterogeneous (heterozygous) wild-type "population," the result being an increased frequency in the sur-
vivors of resistance-conferring genes. This premise permits interpretation on the modern genetic
basis of reasoning.

II) Direct or *ad hoc* response by the adaptation of insect to toxicant in sub-lethal doses (an acquired 2223
character in the Lamarckian sense). Acceptance of this premise would comport the unimportance to
tolerance development of the heterogeneity (or homogeneity) of the original colony or "population."

b) Experiment, generally, is in complete support of premise I, for instance in *Drosophila melanogaster*: 3057,2223

(1) Rate of development of tolerance in the face of DDT-exposure depended on the relative proportion of 3057
resistant and susceptible individuals in the initial wild-type colony and the intensity of the selection 2223
as measured by the DDT-dosage level (i.e., the proportion of the exposed "population" killed at each
exposure).

(2) Ability of a stock to yield DDT-R biotypes is related to the genetic variability of the original stock. 2223
The failure of certain highly inbred laboratory "populations" to yield resistant biotypes indicates that
certain genes must be present in the original stock as a basis for tolerance selection. Lamarckian
adaptation by direct physiological response *ad hoc* should be possible to the most homogeneous as well
as to the most heterogeneous "populations."

(3) Tolerance ordinarily increased most rapidly during the first few months of selection exposure, ulti- 2223
mately reaching a "plateau level" which differed for each original stock subjected to the course of 658
exposure. Resistant biotypes, derived from different original stocks, differed among each other and 2512
from the control stocks. In these experiments resistance level did not remain static; some (3) toler-
ant biotypes later declined in tolerance despite continued exposure to DDT. This last indicated
(among other things) that homozygosity for resistance had not been attained and the possibility that
certain adverse selective factors may be associated with high insecticide tolerance to confer upon the
insecticide resistant biotype a generally negative survival value.

c) *Summary*: [Refs.: 3057, 2223, 2231, 353, 373, 2075, 2095, 2091, 736, 1597, 737, 1411, 1412, 2263, 658, 3131, 789, 3394]

(1) From a "population" heterogeneous with respect to tolerance and susceptibility a toxicant (as an agent of the environment) selects for survival individuals which possess factors making for tolerance. If these factors are genetic they are transmissible to the progeny. As the breeding group, under pressure of selection, becomes restricted to tolerants the frequency of the resistance-conferring genes increases in the breeding group and the drive of selection may lead to a biotype homogeneous for the factors in question. Such a biotype having attained full homozygosity for resistance-conferring genes, barring mutation, should reach a resistance plateau and no further selection should enhance the

tolerance. Providing the tolerance-conferring genes carry no negative survival value in other respects, for instance behavior, breeding potential, developmental rate, physiological requirements, etc., in an environment of which the toxicant is a factor the tolerant biotype(s) should prevail.

(2) Among insect "populations" in nature mutants have arisen at random. Among such mutations it may be presumed that there are those which confer increased (or decreased) tolerance to a toxicant. Such mutations are tested for survival only when the toxicant is a factor of the environment unless they comport other selective advantages or disadvantages concomitantly. Such mutations are by chance and are not ad hoc in response to the toxicant in less than lethal doses nor does any evidence support that a toxicant (even though mutagenic) induces mutations conferring specific adaptation to itself.

(3) The foregoing explanation necessarily oversimplifies the case. The genetics of tolerance are not fully understood and additional reference to genetical experiment and theory generally is essential.

BIOCHEMICAL FACTORS AND INSECTICIDE RESISTANCE

1) In the section on DDT (q.v.) consideration has been given to the metabolism of DDT in resistant and non-resistant *Musca* biotypes and attention is called to that treatment of the data.

2) Some work has been done which demonstrates the ability of lindane-R *Musca* and the ability of certain toxaphene-R and chlordane-R strains to detoxify lindane, toxaphene and chlordane effectively as compared with susceptible biotypes. The following references supply the appropriate details: Refs. 420, 736, 319, 2415, 1562.

QUANTITATIVE DATA ILLUSTRATIVE OF INSECTICIDE RESISTANCE (Also see Refs. 420, 421, 736, 2094, 2096, 2097) 373

1) DDT tolerance, tolerance of insecticides other than DDT, cross tolerance evidences; Topical LD$_{50}$ 24 hrs. μg/g for *Musca domestica*; toxicants in acetone solution:

Biotype of *Musca domestica*	Generations of Exposure to Insecticide; Adults, Larvae	Biotype Origin	LD$_{50}$ Topical (μg/g) For				
			DDT	Methoxychlor	Lindane	Chlordane	Dieldrin
Laboratory-I* (non-R)	0	NAIDM	16.8	49.95	1.7	8.2	1.1
Laboratory-II (non-R)	0	U. of Indiana	8.96	50.0	2.2	4.2	0.87
DDT-I (R)	21	Laboratory-I	13,040.0	721.0	5.52	12.1	2.4
DDT-W (R)	3 yrs (field)	Wild type	505.5	76.4	2.1	4.1	1.3
DDT-III (R)	4 yrs (field)	Wild type	1,350.0	461.2	2.2	5.1	1.0
Methoxy-I** (R)	21	Laboratory-I	19.2	9,176.0	3.75	12.9	1.49
Lindane-I (R)	21	Laboratory-I	18.2	--	33.4	14.7	2.66
Multi-I (R)	8	DDT-I	18,728.0	14,586.0	8.56	15.6	2.33
Dieldrin-I (R)	21	Laboratory-I	15.1	--	2.8	11.2	6.31
Chlordane-I (R)	21	Laboratory-I	16.2	--	2.2	10.7	1.9
Para-oxon-I (R)	8	Laboratory-I	--	--	--	--	--
Pyro-(pyrethrin) I (R)	21	Laboratory-I	34.7	--	7.7	19.9	3.98
Multi-III (R)	8	Methoxy-I	135.1	1,334.0	25.0	66.6	8.3
Multi-IV (R)	4	Methoxy-I	18.8	9,277.0	7.38	18.2	--
Multi-II (R)	4	Methoxy-I	20.0	10,444.0	5.3	--	7.1
Toxaphene-I (R)	21	Laboratory-I	--	--	--	--	--

			LD$_{50}$ Topical (μg/g) For			
			Pyrethrins + Piperonylbutoxide (1:10)	Toxaphene	DDT 16.6%, Methoxychlor 83.4%	Paraoxon
Laboratory-I* (non-R)	0	NAIDM	56.8	29.16	47.2	2.6
Laboratory-II (non-R)	0	U. of Indiana	49.1	32.2	--	1.9
DDT-I (R)	21	Laboratory-I	88.7	73.0	466.6	3.8
DDT-W (R)	3 yrs (field)	Wild type	74.8	38.4	--	--
DDT-III (R)	4 yrs (field)	Wild type	65.8	--	--	--
Methoxy-I** (R)	21	Laboratory-I	80.2	38.2	95.6	2.3
Lindane-I (R)	21	Laboratory-I	62.5	66.3	--	--
Multi-I (R)	8	DDT-I	89.9	76.4	4,851.1	6.2
Dieldrin-I (R)	21	Laboratory-I	--	--	--	--
Chlordane-I (R)	21	Laboratory-I	--	--	--	--
Para-oxon-I (R)	8	Laboratory-I	--	--	--	10.06
Pyro-(pyrethrin) I (R)	21	Laboratory-I	258.7	--	--	--
Multi-III (R)	8	Methoxy-I	81.6	--	--	--
Multi-IV (R)	4	Methoxy-I	--	--	--	--
Multi-II (R)	4	Methoxy-I	--	--	--	--
Toxaphene-I (R)	21	Laboratory-I	--	39.6	--	--

*Larvae of Laboratory-I tolerated up to 80 ppm DDT, 320 ppm methoxychlor, 160 ppm lindane, 5 ppm chlordane and 1.2 ppm dieldrin incorporated in larval medium.

**Note that Methoxy-I although greatly resistant, after 21 generations of exposure to methoxychlor, remained approximately the same in susceptibility to DDT as its parent strain. Also consult Ref. 179.

(2) Further evidences of DDT-tolerance and cross-tolerance in Musca domestica after Ref. 2231:

Insecticide	LD$_{50}$ Topical (μg/♀ Fly) 24 Hrs For						
	DDT non-R biotypes		DDT-R biotypes				Prolan-R biotype
	Laboratory	Rome	Bellflower	Pollard	Italian	Sardinia	
DDT	0.033	0.44	11	100	6.8	7.2	100
DBrDT	.039	.6	40	-	8.3	7.6	-
DFDT	.1	-	4	1.2	-	-	-
2,2-Bis-(p-tolyl)-1,1,1-trichloroethane	.16	1.45	0.7	2.7	28.4	3.0	-
2,2-Bis-(p-ethylphenyl)-1,1,1-trichloroethane	.11	-	1.2	2.7	-	-	-
Methoxychlor	.068	.48	0.96	1.4	5.0	1.08	-
DDD	.13	.88	60	100	6.6	7.8	-
Lindane	.01	.024	0.08	0.25	0.02	0.2	2.5
Heptachlor	.032	-	0.06	1.5	-	-	-
Aldrin	.044	.036	0.076	0.78	0.04	1.2	-
Dieldrin	.031	.024	0.05	0.86	0.028	1.2	-
Toxaphene®	.22	.36	0.62	3.4	0.36	3.6	-
Chlordane	-	.16	-	-	0.15	11.2	-
Prolan®	.095	-	0.15	0.11	-	-	50-100
Bulan®	.15	-	0.18	0.11	-	-	6
Parathion	.015	-	0.02	0.023	-	-	0.032
Pyrethrins	1.0	.28	0.94	1.6	1.4	0.24	6
Allethrin	.43	-	0.97	0.5	-	-	-
Isobornyl thiocyanoacetate (Thanite®)	-	3.2	-	-	3.6	3.4	-
β-Butoxy-β'-thiocyanodiethyl ether (Lethane 384®)	-	2.4	-	-	2.6	2.8	-

(3) DDT tolerance of Musca domestica biotypes and tolerance to other insecticides: (Also consult Ref. 1831.) 2098

Insecticide	LD$_{50}$, 24 Hrs Topical (μg/Fly) For				
	Laboratory Biotype Non-R	Riverside	Ontario	San José	Bellflower
		DDT-R Biotypes			
DDT	0.02	0.5	0.5	0.7	10.0
DDD	.1	-	-	-	20.0
Methoxychlor	.07	.3	.3	.3	1.0
Toxaphene®	.2	.5	.5	.4	0.6
Lindane	.01	.06	.05	.05	0.08
Heptachlor	.03	.07	.07	.07	0.06
Pyrethrins	1.0	2.0	2.0	2.0	1.0

(4) Toxicity of several insecticides for 2 biotypes of Musca domestica, Orlando DDT-non R and Auburn DDT-R (ca. 14 times as tolerant of DDT as is Orlando DDT-non R): 2110 2411

Insecticide	LD$_{50}$ 24 Hrs, Topical (μg/Fly),(μg/g) In Acetone Solution			
	Orlando, DDT-non R		Auburn, DDT-R	
	μg/Fly	μg/g	μg/Fly	μg/g
DDT	0.45 (0.42 - 0.6)*	27.5	6.4 (5.5 - 7.2)*	303.4
Methoxychlor	1.93 (1.33 - 2.33)	127.9	2.33 (2.03 - 2.53)	135.18
Lindane	0.75 (0.5 - 1.25)	51.3	1.25 (1.0 - 1.57)	80.7
Chlordane	42.0 (42.0 - 84.0)	3,586.8	29.0 (12.0 - 57.0)	2,791.3
Heptachlor	11.0 (8.75 - 15.0)	955.68	13.0 (11.0 - 17.0)	855.79
Endrin	1.9 (1.55 - 2.32)	104.4	2.1 (1.75 - 2.5)	118.9
TEPP	0.19 (0.16 - 0.27)	10.4	0.24 (0.16 - 0.35)	13.6
Malathion	0.87 (0.72 - 1.0)	47.8	1.07 (0.92 - 1.27)	57.3
Chlorthion	0.21 (0.19 - 0.25)	16.89	0.14 (0.1 - 0.2)	10.52
Diazinon	0.1 (0.09 - 0.11)	6.15	0.06 (0.05 - 0.07)	3.01
American Cyanamid 4124	0.02 (0.02 - 0.03)	1.73	0.03 (0.03 - 0.03)	2.75

*Fiducial limits 0.95%; overlap in fiducial limits indicates no significant difference in toxicity for the two tested strains.

(5) Toxicity of DDT and other compounds. Association of susceptibility and resistance with other physiological characteristics as shown by LD$_{50}$ values (as μg of insecticide deposited on surface of holding vial from petroleum ether solution with mortality taken at 24 hours following a 1-hour exposure in test vials) for the Super-Laton strain and two substrains (early pupating and late pupating colonies) established by selection. Subscripts indicate the generation(s) tested. 2198

(5) Toxicity of DDT and other compounds (Continued)

Substrain	LD$_{50}$ (μg/vial) 24 Hrs After Exposure For						
	DDT	DDD	Methoxychlor	Lindane	Aldrin	Dieldrin	Pyrethrins
Super-Laton Check	18_{26}	35_{27}	$16_{16,27}$	1.0_{2}	$0.4_{23,24}$	0.4_{24}	13_{27}
Super-Laton Early Pupating	12_{22}	$30_{21,25}$	$14_{24,25}$	0.7_{20}	0.4_{20}	0.4_{20}	$9_{25,26}$
Super-Laton Late Pupating	110_{20}	$290_{19,23}$	38_{19}	$0.8_{17,18}$	$0.4_{19,22}$	$0.5_{19,20}$	13_{22}
B Check	11.5_{8}	38_{3}	14	-	0.4_{3}	0.3_{3}	11.5_{3}
B Early Pupating	8.5_{10}	$39_{9,10}$	$17_{9,10}$	0.4_{10}	0.3_{9}	0.3_{10}	$14_{9,10}$
B Late Pupating	30.0_{9}	90_{9}	$18_{8,9}$	0.7_{8}	-	-	$14_{8,9}$

(6) Evidence that larvae, reared from biotypes of Musca domestica DDT-R, Chlordane-R, Dieldrin-R, and Methoxychlor-R as adults, are also resistant: 1326

Insecticide	mg/k Medium	% Mortality Of Larvae Of 3 Wild-Collected Biotypes			
		Trenton	Darago	Enders	Laboratory Strain (Control)
Dieldrin	2.5	0	-	-	90
"	10.0	10	75	-	100
"	50.0	0	85	-	-
"	100.0	10	100	-	-
Aldrin	10.0	40	65	30	60
"	50.0	-	95	75	-
"	100.0	-	95	95	-
Heptachlor	10.0	25	80	-	100
Chlordane	10.0	-	80	-	95
DDT	10.0	40	-	-	65
Methoxychlor	10.0	40	-	-	45

(7) Toxicity of insecticide vapors and residues for resistant and non-resistant biotypes of Musca domestica: 3320

Biotype	Lethal Time$_{50}$ (Minutes) For						
	Chlordane	Lindane		Dieldrin		Aldrin	DDT
	Vapors	Vapors	Residues	Vapors	Residues	Vapors	Residues
Non-R	33	25	10.9	40	<1	<15	9.0
Orlando No. 1 *	69	58	16.4	110	9.1	23	ca. 1440
LDD **	347	173	65.6	550	>120	158	>240
Ballard ***	380	316	229.3	550	-	96	343.4

*Exposed only to DDT for which the biotype showed high tolerance with some cross tolerance for lindane, dieldrin and chlordane.

**From a "population" in a dairy which DDT, dieldrin or lindane would not control. Resistance maintained by continuous exposure to residues in adult holding cages.

***A wild strain originating in a dairy treated with space and residual lindane with relative ineffectiveness of control.

EVIDENCES OF THE ORIGIN OF TOLERANCE IN FIELD "POPULATIONS" OF MUSCA DOMESTICA EXPOSED TO VARIOUS INSECTICIDES

1) Rise of tolerance in Musca domestica natural "populations" from DDT treated dairies: * 1171

Dairy	Insecticide	Season (1950)	Lethal Time$_{50}$ (Minutes); Exposure to Residues	
			Dairy Musca	Laboratory Colony Musca
Lakemont	DDT suspension	Spring	89	6
"		Fall	>240	1.2
"		"	187	1.6
"	Chlordane emulsion	Spring	16	16
"	(from acetone solution)	Fall	>240	10
		Fall	403	7.9
"	Lindane (acetone solution)	Fall	65	3.1
Ballard	DDT suspension	Spring	42	6
"	Toxaphene suspension	Spring	46	81
"	Toxaphene (acetone solution)	Fall	>240	3.7
"	Lindane (acetone solution)	Fall	53	3.4
Knight	DDT suspension	Fall	195	2.9
"	Lindane (acetone solution)	Fall	71	0.8
Judge	DDT suspension	Fall	109	1.6
"	Lindane (acetone solution)	Fall	12	0.8

---

* In 1947 there was no evidence of tolerance. In 1948 tolerance was noted in some places; for instance, fall

flies were 4 times as tolerant of DDT as spring flies. In 1949 the average Lethal Time$_{70}$ of flies from 18 barns was 34.4 minutes vs. 3.2 minutes for the laboratory colony; insects were more than twice as resistant as the laboratory strain to methoxychlor, lindane, toxaphene and dieldrin.

In 1951 resistance of ♀ Musca domestica from several dairies to residual lindane and DDT insecticides alone and with synergists:

Dairy	Month of Collection	Lethal Time$_{50}$ (Minutes); Exposure to Residues			
		Lindane		DDT	
		Alone	With Synergist	Alone	With Synergist
Lakemont (1)	June	14	4	239	80
"	Sept.	65	52	193	95
Lakemont (2)	June	10	26	140	-
"	Sept.	143	167	361	106
Ballard (2)	June	27	29	>240	-
"	Aug.	46	38	>240	126
"	Sept.	229	284	343	321
Ballard (3)	June	17	12	83	47
"	July	36	20	>240	160
"	Aug.	62	61	164	123
"	Sept.	274	202	638	180
How-Ann	June	8	<5	96	58
"	Aug.	20	20	>240	84
"	Oct.	63	75	>240	57
Laboratory Colony	June	3	3	15	>20
"	July	5	2	8	12
"	Sept.	11	6	9	18

2) Tolerance in field "populations" of Musca domestica. As control with insecticides grew progressively poorer through the season until it became completely unsatisfactory 3 field strains were tested against a non-R laboratory colony by exposure to residues on plywood panels: 1326

Insecticide	mg/in²	% Mortality For Biotypes At Exposure Time (Hrs) Shown									
		Trenton			Darago			Enders			Laboratory
		.25	1	2	.25	1	2	.25	1	2	.25
Dieldrin	0.1	-	4	6	-	0	4	-	0	0	100
Aldrin	0.1	-	3	0	-	0	5	-	7	9	98
Heptachlor	0.1	-	3	9	-	24	22	-	-	-	75
Chlordane	0.1	-	0	8	-	0	0	-	-	-	46
DDT	1.0	-	4	2	-	-	-	-	-	-	100
Methoxychlor	1.0	-	9	14	-	-	-	-	4	12	25
Control	0		0			0			0		0

3) Laboratory tests with Musca domestica collected in barns where control with residual insecticides had proved a failure; in each instance the insecticide in capital letters* is the substance used in the barn of biotype origin from 1949 to 1952. Flies exposed to the insecticides on plywood test panels: 1383

Barn Of Origin For Musca domestica	Insecticide On Test Panel	Exposure Time (Minutes)	% Mortality
I	LINDANE *	15	0
	Methoxychlor	15	0
	DDT	15	0
II	LINDANE *	15	0
	Methoxychlor	15	3.6
	DDT	15	3.6
III	METHOXYCHLOR *	15	4.1
	Lindane	5	10.2
	DDT	15	7.3
IV	METHODYCHLOR*	15	3.6
	Lindane	5	2.9
	DDT	15	7.4
V	CHLORDANE *	15	2.2
	DDT	15	0
VI	CHLORDANE *	15	5.0
	DDT	15	10.0
VII	DIELDRIN *	15	4.2
	DDT	15	0
Laboratory Colony (non-R)	Lindane	5	100
	Methoxychlor	15	100
	DDT	15	84
	Chlordane	15	100
	Dieldrin	15	100
Control	--	--	4

INSECTICIDE TOLERANCE IN PEDICULUS HUMANUS CORPORIS

1) Effectiveness of insecticides in cloth patch tests of dusts in pyrophyllite or on patches impregnated with insecticides in solution vs. the DDT-R (Korean) biotype of P. humanus corporis: 915

Insecticide	% Mortality After 24 Hrs Exposure To Indicated Concentration of Insecticide									
	% Concentration									
	1.0%	0.5%	0.1%	0.05%	0.01%	0.005%	0.0025%	0.001%	0.0005%	0.0001%
DDT	17	-	-	-	-	-	-	-	-	-
Methoxychlor	20	-	-	-	-	-	-	-	-	-
Perthane	80	-	-	-	-	-	-	-	-	-
DDD	100	97	60	-	-	-	-	-	-	-
Allethrin	-	-	100	100	62	-	-	-	-	-
Pyrethrins	-	-	100	100	65	-	-	-	-	-
Toxaphene®	-	-	-	100	88	62	-	-	-	-
Chlordane	-	-	-	-	100	96	90	48	-	-
Lindane	-	-	-	-	-	100	95	80	-	-
Aldrin	-	-	-	-	-	-	100	100	80	60
Dieldrin	-	-	-	-	-	-	100	100	90	40

Korean Pediculus humanus capitis remained DDT-susceptible. Susceptibility of DDT-R (Korean) Pediculus humanus corporis to DDD, Allethrin, Pyrethrins, Toxaphene, Chlordane, Lindane, Aldrin and Dieldrin proved equal to that of the Orlando Laboratory Strain (U.S.). In the field the DDT-R biotype was controlled with pyrethrum and allethrin powder formulations, reduction with one treatment being good and eradication achieved in 3 - 6 treatments. Treatments given every 5 days with a subsequent weekly treatment if reinfestation persisted.

INSECTICIDE TOLERANCE OF BLATTELLA GERMANICA

1) Comparative toxicity of some insecticides in dipping tests for the chlordane-R and chlordane-non-R biotypes of Blattella germanica; LC_{50} and LC_{90}, as cc/l for chlordane and TEPP g/l for lindane: 1259

Insecticide	Sex	Non-R Biotype		Chlordane-R Biotype		Order Of Resistance At	
		LC_{50}	LC_{90}	LC_{50}	LC_{90}	LC_{50}	LC_{90}
Chlordane	♂	0.0034	0.0063	0.38	2.1	111.7	333.3
"	♀	.0165	.0476	4.55	14.87	275.7	312.3
Lindane	♂	.0103	.0155	.0595	.076	5.7	4.9
"	♀	.0242	.0430	.094	.185	3.8	4.3
TEPP	♂	.0575	.11	.112	.165	1.9	1.5
"	♀	.153	.395	.265	.512	1.7	1.2

2) Toxicity of chlordane (dipping tests in aqueous suspensions of acetone-EMCOL H 65 A chlordane solutions) for chlordane-non-R and chlordane-R biotypes of Blattella germanica: 1260

Biotype	Sex	LC_{50} (cc/l)	LC_{90} (cc/l)	Resistance Ratio At	
				LC_{50}	LC_{90}
Non-R	♂	0.0041	0.0192	1.0	1.0
"	♀	.0117	.04	1.0	1.0
Chlordane-R	♂	.340	1.5	84.1	78.1
"	♀	3.550	10.7	303.4	251.8

3) Toxicity of certain insecticides for the Non-R and Chlordane-R (Corpus Christi) biotype of Blattella germanica by injection; adult ♀ insects: 431

Insecticide	Non-R Biotype		Chlordane-R Biotype		LD_{50} R / LD_{50} Non-R	LD_{90} R / LD_{90} Non-R
	LD_{50} ($\mu g/g$)	LD_{90} ($\mu g/g$)	LD_{50} ($\mu g/g$)	LD_{90} ($\mu g/g$)		
Aldrin	26.46	70.06	127.61	1113.6	4.82	15.89
Chlordane	81.29	144.27	1117.5	4648.8	13.76	32.22
Dieldrin	6.59	17.35	68.37	502.49	10.34	28.54
Heptachlor	9.07	19.85	174.21	1509.3	19.21	76.04
Lindane	1.01	2.57	23.13	75.02	22.72	29.19

4) Certain insecticides vs. R and Non-R biotypes of Blattella germanica; by topical application to adult ♀ insects: 1012

Insecticide	Non-R	DDT-R		Chlordane-R	
	LD_{50} 48 hrs μg/insect	LD_{50} 48 hrs μg/insect	Degree Resistant	LD_{50} 48 hrs μg/insect	Degree Resistant
DDT	13.5	25.0	1.9	19.0	1.4
Chlordane	2.3	4.1	1.8	250.0	108.6
Dieldrin	0.5	0.62	1.2	34.0	68
Diazinon	0.33	0.78	2.4	0.4	1.2
Allethrin (+ synergist)	0.76	1.3	1.7	1.0	1.3

5) Behavior toward insecticides of the insecticide-R (Corpus Christi) biotype of Blattella germanica compared with the normal biotype. The insecticide-R biotype is able to survive in environments adequately treated with 2% chlordane (% mortality 48 hrs of Corpus Christi by direct spray of 2% chlordane = 6.2%, of the laboratory (normal) biotype = 100%). 1465

Insecticide	(mg/k)	% Mortality, Topical Application By Measured Drop Method (Acetone Solution)			
		Laboratory Biotype		Corpus Christi Biotype	
		♂	♀	♂	♀
Chlordane	2.5	0	10	-	-
"	5	0	0	-	-
"	10	10	10	10	0
"	20	100	40	-	-
"	40	-	-	0	0
"	160	-	-	0	0
"	640	-	-	20	0
"	2560	-	-	80	20
Lindane	10	70	70	-	-
"	20	100	100	0	10
"	30	100	100	-	-
"	40	100	100	-	-
"	60	-	-	30	50
"	120	-	-	90	70
"	480	-	-	100	100
"	1420	-	-	100	100
DDT	5	30	20	-	-
"	10	10	10	0	0
"	20	20	10	0	0
"	40	30	30	0	0
"	80	80	70	10	0
"	160	100	80	60	0
"	640	-	-	80	80
"	2560	-	-	100	80

RESISTANCE TO INSECTICIDES IN SOME MOSQUITO "POPULATIONS"

1) Laboratory tests of Aëdes taeniorhynchus and Aëdes sollicitans, larvae (4th instar): 1765

Insecticide	% Mortality 48 Hrs At The Concentrations (ppm) Indicated													
	Larvae from marshes occasionally DDT-treated							Larvae from marshes intensely DDT-treated						
	.05	.025	.01	.005	.0025	.001	.0005	.05	.025	.01	.005	.0025	.001	.0005
EPN®	-	100	100	100	100	76	51	-	100	100	100	62	34	-
Dieldrin	-	100	100	95	71	59	-	-	100	90	34	16	8	-
Heptachlor	-	100	100	96	61	54	-	-	100	100	84	24	-	-
Parathion	-	100	100	93	54	22	-	-	-	-	-	-	-	-
Aldrin	-	100	99	87	68	53	-	-	100	82	26	18	16	-
Lindane	-	100	98	69	59	42	-	-	72	36	34	26	16	-
Toxaphene®	-	100	89	64	56	38	-	-	-	98	50	30	24	-
Chlordane	-	100	81	39	28	24	-	-	-	-	-	-	-	-
DDT	100	92	66	62	45	-	-	78	56	38	34	24	-	-
Malathion	100	66	37	34	37	-	-	52	40	32	30	22	-	-
NPD	94	74	54	47	41	-	-	42	26	12	6	0	-	-

Small plot field tests with various insecticide emulsions, conducted in a region (Cocoa Beach, Brevard County, Florida) previously intensely treated with DDT (1945 - 1949) and BHC (1950 - 1952):

Insecticide	% Reduction In 4th Instar Larvae Of A. taeniorhynchus, A. sollicitans In 24 Hrs At					
	0.1	0.05	0.025	0.01	0.005	0.0025
	Lbs/acre					
EPN®	-	100	100	99	91	71
Parathion	-	100	100	100	73	73
Heptachlor	-	100	100	92	23	-
Dieldrin	-	100	100	93	-	-
Lindane	-	100	89	65	-	-
Chlordane	100	100	69	0	-	-
DDT	100	90	71	21	-	-
Malathion	95	98	6	-	-	-
NPD	12	19	0	-	-	-
TEPP	49	0	0	-	-	-

APPEARANCE OF APPARENTLY TOLERANT BIOTYPES OF MUSCA DOMESTICA ON DANISH FARMS WHERE CERTAIN ORGANIC PHOSPHATE INSECTICIDES HAVE BEEN USED FOR FLY CONTROL AS RESIDUAL SPRAYS, BAITS, OR ON IMPREGNATED GAUZE STRIPS AGAINST BIOTYPES RESISTANT TO CHLORINATED HYDROCARBON INSECTICIDES 1761

P = parathion, D = diazinon, B = Bayer 21/199, e = emulsion spray, s = impregnated gauze strips, * = reports of failing effectiveness.

Biotype	Collected In	Exposure In Field To Organic Phosphates In				LD$_{50}$, Topical, µg/♀ Fly For		
		1952	1953	1954	1955	Bayer 21/199	Diazinon	Parathion
Laboratory types 9,17	1949-50	0	0	0	0	(.02 - .06)	(.03 - .04)	(.015 - .023)
Jutland 74	July 1955	?	Pe	Pe	Pe	1.7	0.11	0.06
Jutland 79	July 1955	?	Pe	Pe	Ps	(5 - 11)	0.13	0.09
Zealand 98	Aug. 1955	0	0	D	B*	0.9	-	0.03
Zealand 127	Sept. 1955	0	Ps	D	B*	0.9	0.17	0.05
Zealand 129	Sept. 1955	0	Ps	D	B*	0.5	0.09	0.05
Zealand 149	Oct. 1955	Ps	Ps	D	D*	0.6	0.3	0.06
Zealand 150	Oct. 1955	0	Ps	D	D*	1.3	0.5	-
Fünen 151	Nov. 1955	0	0	D	D*	0.06	0.13	0.04

1) Development of tolerance to chlorinated hydrocarbon insecticides on a Danish farm (at Tillitze, Lolland) under conditions in which flies (Musca domestica) were breeding freely in calf-boxes in insecticide-treated cow-sheds: 1762

Date	Insecticide Used	Dosage	Sprayings (No.)	Estimated Degree of Control
1945	DDT	-	?	ca. 100%
1946 - 1947	DDT	-	Several	decreasing
1948	DDT	-	?	ca. 0%
"	BHC	-	?	ca. 100%
1949	BHC	0.1-2.0 g/m^2	2	ca. 25%
"	Chlordane	1 - 2 g/m^2	2	ca. 100%
1950 May	Chlordane	1 g/m^2	1	ca. 75%
" June	Chlordane	2 g/m^2	1	ca. 50%
" July	Chlordane	2 g/m^2	2	ca. 25%
" "	Toxaphene	2 - 4 g/m^2	2	ca. 0%
" "	BHC	0.5 g/m^2	1	ca. 0%
" "	Chlordane	2 g/m^2	1	ca. 25%

Several highly DDT-R field biotypes showed similar high methoxychlor, DFDT and DDD tolerance but were BHC, chlordane and toxaphene susceptible to same degree as the laboratory susceptible strain. From a farm where DDT was used without yielding control for 2 years, then treated with BHC for one year, arose a highly BHC-R biotype with an LD$_{50}$, topical of 7 µg gamma isomer/fly, 200 times greater than the LD$_{50}$ for the BHC susceptible laboratory strain and 10 times greater than the LD$_{50}$ for the Bruce-Decker Lindane-R strain.

2) Some baits tested for the control of certain chlorinated hydrocarbon-R biotypes of Musca domestica: 1095

Toxicant	Concentration (%)	Formulated in Water Without Malt		Formulated in Water With 5% Malt	
		% KD$_{24\,hrs}$	% Kill$_{24\,hrs}$	% KD$_{24\,hrs}$	% Kill$_{24\,hrs}$
TEPP	0.2	78	78	100	100
Sodium fluoroacetate	1.0	98	96	100	100
Sodium arsenate	2.0	100	100	100	100
Sodium arsenite	2.0	88	90	100	100
Sodium fluosilicate	5.0	82	82	62	82
Ammonium bifluoride	5.0	8	8	68	100
Sodium fluoride	5.0	6	9	62	100
Nicotine sulfate	5.0	35	40	7	15

SOME RECENT FIELD REPORTS OF INSECT RESISTANCE TO INSECTICIDES

1) Thrips tabaci: Resistance in field reported for dieldrin, heptachlor and toxaphene in lower Rio Grande Valley. 2602

2) Myzus persicae: Reported difficult to control (previously very susceptible) in various regions of Washington State using parathion, malathion, TEPP, Metacide® ; Systox® continues to control. 103

3) Carpocapsa pomonella: In certain New York orchards appears to show DDT-R as measured by failure to control during 2 seasons with treatments successful in 6 prior seasons. 1201 1361

4) Chromaphis juglandicola: Is reported to show a parathion-R biotype at San José, California. 2256

5) Lygus hesperus: Has shown DDT tolerance on alfalfa in Northern California with insects at harvest being 3 - 4 times as tolerant of DDT as those from untreated fields or as they were at the season's beginning. 72

6) Erythroneura variabilis: Has manifested DDT-R "populations." 1363,192

7) Pieris rapae: Has shown itself DDT-R in certain "populations"; with cross tolerance for Perthane®, DDD and methoxychlor. 2169

8) Trichoplusia ni: DDT-R biotypes reported. 1440

9) Epilachna varivestis: Resistance to rotenone shown by "populations" in certain bean-growing regions of North Carolina: 332

Rotenone Dust Conc. (%)	% Kill 48 Hrs, 3rd, 4th Instar Norfolk, Va. Insects (non-R)	 Mills River, N. C. Insects (R)
1.0	100	52
.5	89	19
.25	68	12
0	3	3
	Norfolk (field collected)	Mills River F_3 (laboratory reared)
100	100	34
0.5	73	11
0.25	36	5
0.0	1	7

% Kill of 3rd, 4th Instar Larvae On Leaves Dipped In Rotenone Emulsions

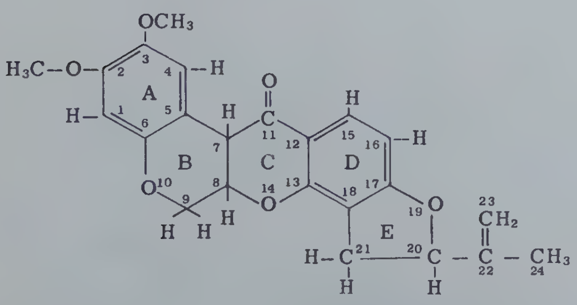
Conc.(%)	Norfolk Strain	Mills River Strain
0.08	38	18
.04	22	7
.02	27	6

157

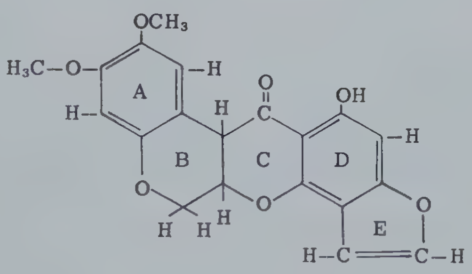
ROTENONE; "ROTENOIDS"

(Derrin, Nicouline, Tubatoxin; in a broad sense: Derris, Lonchocarpus, Cubé, Tuba, Barbasco or such terms as may be applied locally or in commerce to rotenone and rotenoid containing plants or plant parts.)

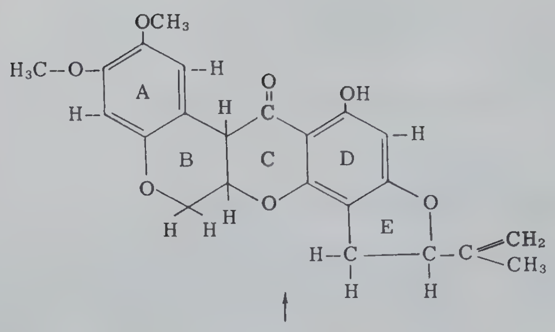
N.B. The formulae appearing below are for the 6 rotenoids (including rotenone, the most active principle) which occur in nature. In each instance, the naturally occurring optical isomer is the laevo-isomer.



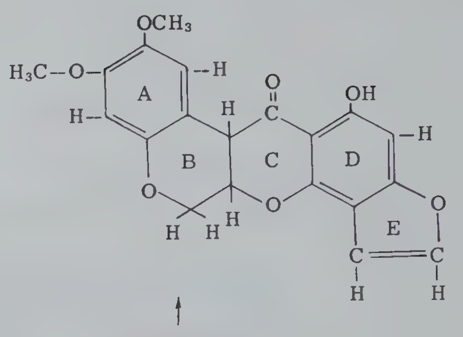
**Rotenone molecular weight 394.41



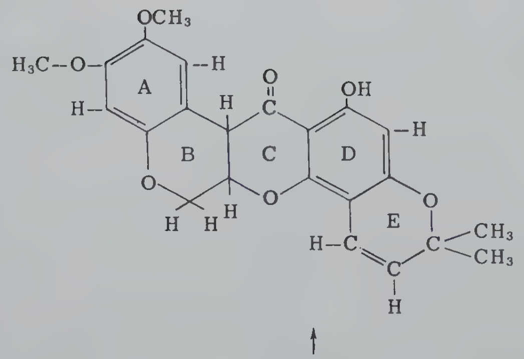
Elliptone



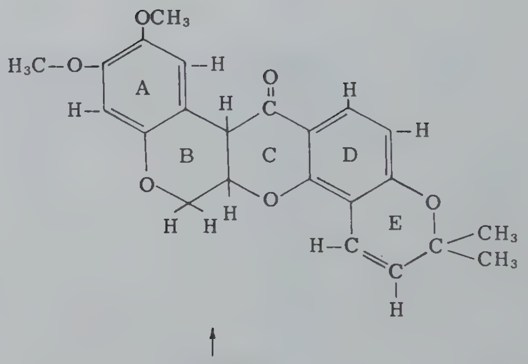
Sumatrol



Malaccol



1-α-Toxicarol



Deguelin

GENERAL [Refs.: 1889, 674, 1801, 353, 2231, 2815, 2226, 1059, 757, 129, 2120, 2426, 1139, 2343, 1722, 1580, 2663, 1138]

Rotenone and the other rotenoids constitute the more or less insecticidally active principles (of which rotenone is the principal and most important) of certain plants, long known by various primitive peoples as active and potent fish toxicants. The insecticidal properties have been recognized in a systematic way for more than a century. Plants known to yield rotenone and rotenoids are grouped among the following genera, all being of the family Leguminosae:

Genus	Number Of Known Rotenone Bearing Species
Tephrosia (= Cracca)	21
Derris	12
Lonchocarpus	12
Millettia	10
Mundulea	2

The chief commercial sources of rotenoids and rotenone are Derris elliptica, and Derris malaccensis (whose dried parts are known as derris), Lonchocarpus utilis, and Lonchocarpus urucu (whose dried parts in commerce are known as cubé or timbo). The genus Derris is abundant in Southeast Asia where it has been brought into cultivation and subjected to selection and improvement. Lonchocarpus spp. are of South American origin. These plants may be employed in a crude form as ground roots (that part in which the insecticidal principles chiefly reside) as resins, roughly or crudely extracted from the plants, or as pure, crystalline rotenone, isolated by purification and solvent extraction from the resins. Not only is rotenone toxic in high degree to a wide range of economic insects, but it possesses the great advantage of leaving behind no toxic residues. As a selective contact insecticide with some degree of acaricidal action, rotenone is, among the natural insecticides of plant origin, of unique value for home garden, horticultural and agricultural uses and for the control of livestock insects: Lice, fleas, warble-fly grubs (and other cattle grubs) and the sheep ked.

The rotenone-bearing plants contain, in addition to the insecticidal fractions in their resins, non-insecticidal resin constituents, for example, sesquiterpene-containing oils, various unknown crystalline fractions and lonchocarpic acid.

Rotenone is completely non-phytotoxic and presents a low hazard to warm-blooded animals.

For evaluations of rotenone-containing plants, their resin differences, relative toxicity, etc., see Refs. 3059, 2130.

PHYSICAL, CHEMICAL

Rotenone is a colorless solid, crystallizing in hexagonal, orthorhombic crystals, odorless, and laevo-rotatory 1726
in solution with organic solvents ($[\alpha]_{D}^{20^\circ C}$ - 231.0° in benzene); m.p. 163°C (a dimorphic form melts at 2231,353
181°C); melting points of the several rotenoids: 129,2120
1720,3002
3047
437
1889

Rotenone	- 163°C	Elliptone	- 159°C	l-α-Toxicarol	- 101°C
Malaccol	- 244°C	Sumatrol	- 188°C	Deguelin	- 165° - 171°C

and Tephrosin (an oxidation product of deguelin) m.p. 197° - 198°C;

virtually insoluble in water (to 15 ppm at 100°C) and soluble to the following g/100 cc solvent at 20°C in organic solvents:

Acetic acid	- 2.4	CS_2	- 1.6	β,β-Dichloroethyl ether	- 7.5	Methanol	- 0.2	Xylene -	
Acetone	- 6.6	CCL_4	- 0.6	Ethylacetate	- 4.8	n-Propyl formate	- 6.0		3.4
Amyl acetate	- 1.6	Chlorbenzene	- 13.5	Ethanol	- 0.2	Trichloroethylene	- 16.5	Water -	
Benzene	- 8.0	Chloroform	- 47.2	Ethyl ether	- 0.4	Toluene	- 6.4		.000016

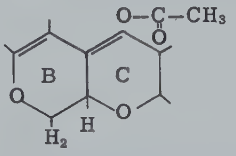
Slightly soluble in petroleum oils; reactive with acetic, dichloroacetic and some other acids; oxidized readily, decomposed and detoxified by exposure to light at a rate proportional to the logarithm of the radiant energy; ca. 100% of the toxicity is lost on exposure to spring sunlight for 5 - 6 days, summer sunlight 2 - 3 days; heat labile: At 100°C 76% of the rotenone and 54% of the total extractives are lost from the crude product in 2 hrs; at 40°C 4.6% of the rotenone and 16% of the total extractives are lost in 30 hrs; the course of degradation by heat: Conversion to a colorless hydroxy- compound which is readily converted to dehydrorotenone (a yellow compound) with spontaneous loss of water, under extreme conditions rotenonone is formed; toxicity is lost completely with conversion to dehydrorotenone; hydrogenation removes the double bond in the side-chain of ring "E" producing dihydrorotenone, a substance still highly toxic.

Rotenone content varies with product and plant source:

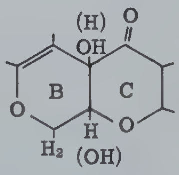
	Average Rotenone (%)	Other Ether Extractives (%)
Derris elliptica	5 - 9	to 31
Derris malaccensis	0 - 4	to 27
Lonchocarpus utilis	8 - 11	to 25

Rotenoid	Product (% Composition) A	B	C
Rotenone	40	20	2 - 5
l-Toxicarol	8	25	50 - 60
l-Deguelin	27	27	12
Sumatrol	-	trace	5 - 15
Fats, Waxes, Acids	10	10	10
Unaccounted For (elliptone? malaccol?)	15	18	8 - 11

In the course of determination of the structure of rotenone various derivatives were identified, for instance, dihydrorotenone and other dihydro derivatives differing from rotenone by saturation of the "E" ring side-chain; in isorotenone the double bond of the "E" ring side-chain is shifted to the "E" ring; acetyl rotenone is an enol acetate in which rings "B" and "C" =



rotenolone is a hydroxyrotenone in which rings "B" and "C"=



Rotenone is compatible with most pesticidal materials but lime is to be avoided.

a) Formulations: 0.75% - 1.0% dusts or the equivalent in sprays for garden crops; Derris or Lonchocarpus root in non-alkaline carriers in ground form, (dusts prepared from extracts rapidly deteriorate); crop dusts, livestock sprays, etc.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) Toxicity for warm-blooded forms varies with the animal, formulation, mode of administration and nature of solvent. Toxicity for animals and man is rather low. Highly toxic to swine according to some reports. 851 1806

1) Acute toxicity for higher animals (Continued)

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Man	or	LD (estimate)	200 mg/subject		2221
Mouse	ip	LD_{100}	10	In ethylene glycol solution.	2827
Rat	or	LD_{80}	100	"	2827
Rat	or	LD_{70}	700		1321
Rat	or	LD_{50}	132	As crystalline rotenone.	1951
Rat	or	LD_{50}	ca. 25	In olive oil solution.	1992
Rat	or	LD_{50}	1000	As solid rotenone, above 60 mesh.	1992
Rat	or	LD_{50}	150	Passing 100 mesh; fats in digestive tract increase toxicity.	1992
Rat	or	LD_{70}	100	As derris powder.	1321
Rat	or	LD_{70}	700	As derris powder; sans rotenone, 21% extractives.	1321
Rat	or	LD_{50}	1500	As derris powder.	1951
Rat	or	LD_{70}	200	As cubé, rotenone 4.7%, total extractives 21.4%.	1321
Rat	ip	LD_{100}	5	In ethylene glycol solution.	2827
Rat	iv	LD	6	In olive oil solution.	2231
Guinea Pig	or	MLD	ca. 200	In ethylene glycol solution.	2827
Guinea Pig	or	MLD	ca. 75	"	1318
Guinea Pig	or	LD_{70}	60	As crystalline rotenone.	1321
Guinea Pig	or	LD_{50}	12	In olive oil solution.	1992
Guinea Pig	or	LD_{70}	75	As derris powder, 9.6% rotenone, 28.5% total extractives.	1321
Guinea Pig	or	LD_{70}	200	As cubé powder, 4.7% rotenone, 21.4% total extractives.	1321
Guinea Pig	sc	MLD	ca. 16	In ethylene glycol solution.	1318
Guinea Pig	im	MLD	ca. 7	"	1318
Guinea Pig	ip	MLD	ca. 20	"	1318
Guinea Pig	ip	MLD	ca. 15		2827
Rabbit	or	LD_{70}	3000	As crystalline rotenone.	1321
Rabbit	or	LD_{70}	600	As derris powder; rotenone 9.6%, total extractives 28.5%.	1321
Rabbit	or	LD_{70}	2000	As derris powder; sans rotenone, 21% extractives.	1321
Rabbit	or	LD_{70}	1000	As cubé powder; rotenone 4.7%, total extractives 21.4%.	1321
Rabbit	ct	LD	>940	As a 10% rotenone solution in dimethyl phthalate.	1952
Chicken	or	MLD	996		673
Chicken (nestling)	or	LD_{50}	1000	For older birds 3000 mg/k.	673
Song Sparrow (nestling)	or	LD_{50}	120		673
Chipping Sparrow (nestling)	or	LD_{50}	120		673
English Sparrow (")	or	LD_{50}	200	For older birds 850 mg/k.	673
American Robin (")	or	LD_{50}	200	10 cabbage worms heavily derris dusted fatal to young robin.	673
Pheasant (various)(")	or	LD_{50}	850	For older birds 1200 mg/k; 65 cabbage worms heavily derris dusted fatal to young.	673
Pig	ct	LD	250cc of spray →	7½ lb derris or cubé (5% rotenone) /80 imperial gallons fatal to 100 lb pig. Highly toxic to swine!	1806
"Warm blooded Animals"	or	MLD	50 - 1500		129
Fish	Medium	LC	0.01 - 0.10ppm	As rotenone. [2751,2899,1335,167,1972,1266, 168]	
Fish	Medium	LC	0.2 - 2 ppm	As derris root. [2751,2899,1335,167,1972, 1266,168]	
Fish	Medium	Toxic dose	0.066 ppm	In small lake which remained toxic 1 month.	2899
Fish	Medium	Harmless	0.015 - 0.06ppm		1972
Daphnia (crustacean)	Medium	LC	0.25 ppm	1 hour exposure.	1972

b) For birds it is reported that ground derris root is 25 times as toxic as the pure rotenone it contains (0.75%). 673

(1) Relative toxicity of rotenone and derivatives for Carrassius auratus (goldfish), and for Rat: [2231]. quoting Refs. 1145, 1142, 1143, 1146, 1141, 1144.

Compound	Goldfish Relative Toxicity (Rotenone = 1)	Rat LD_{50}, Oval
Rotenone	1.0	132 mg/k
Deguelin	0.56	>2000 mg/k

b) Relative toxicity of rotenone and derivatives for Goldfish and for Rat (Continued)

Compound	Goldfish Relative Toxicity (Rotenone = 1)	Rat LD_{50}, Oval
Tephrosin	0.23	-
Toxicarol	0.65	>1500 mg/k
Isorotenone	0.23	-
Dihydrorotenone	1.4	>2000 mg/k
Acetyl rotenone	0.55	-
Acetyl dihydrorotenone	0.5	-
Rotenolone	0.1	-
Acetyl rotenolone	0.11	-
Dihydrorotenolone	0.2	-
Acetyl dihydrorotenolone	0.13	-
Dehydrorotenone	-	>2000 mg/k

2) Chronic toxicity for higher animals:

a) Rat:

(1) In diet at 2 ppm for 2 years: Tolerated without tissue damage. 1953

(2) In diet at 5 ppm for 2 years: Tissue damage in liver, hyperplasia, tumors. 1953

(3) In diet at 25 ppm for 2 years: Growth normal. 1953

(4) In diet at 50 ppm for 2 years: Growth retarded; fatty changes in liver, kidneys. 1953

(5) In diet at 0.625%: Death in 7 - 9 days. 1860

b) Rat receiving Derris powder 9.6% rotenone, 28.6% total extractives:

(1) In diet at 78, 156 ppm for 150 days: Normal growth. 53

(2) In diet at 312 ppm for 150 days: Growth slightly retarded. 53

(3) In diet at 1250, 2500, 5000 ppm: Death; with liver, kidney pathology. 53

c) Other mammals: Derris powder 9.6% rotenone, 28.6% total extractives:

(1) Dog, receiving in diet 400 ppm: Stunted growth. Older dogs (full growth) no effect. 53

(2) Rabbit, receiving orally 30 mg/k/day: No effects on growth. 53

(3) Rabbit, receiving orally 60 mg/k/day: Growth retardation; cumulative effect. 53

d) Dermal effects: Irritating to skin and conjunctiva on direct contact with rotenone or derris dusts.

3) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:

a) Pure rotenone is characterized as having toxic properties near those of DDT as an acute poison but it is not stored in the body fat and the chronic hazard is deemed unimportant. Residues are rapidly rendered harmless by exposure. 851

b) Rotenone brings about a numbing and anaesthesia of the oral mucosa and dusts of derris irritate the conjunctivae intensely. 53

c) Respiration is first stimulated, then depressed completely, by rotenone and in acute poisoning continuous convulsive seizures follow the initial respiratory stimulation. 851, 53

d) Poisoned dogs and rabbits manifested serious hypoglycaemia and various accompanying signs. 53

e) General histopathological signs produced in animals by chronic feeding of derris dusts (9.6% rotenone, 28.6% total extractives) at high levels, (312, 1250, 2500, 5000 ppm) included: Mild to moderate hepatic periportal lymphatic infiltration, focal necrosis at hepatic lobular mid-zone, glomerular and intertubular renal hyperaemia. 53

f) Dihydrorotenone at 10 and 20 ppm for 400 days: No histological change; 40 ppm: Growth retard; at 40 - 320 ppm: Progressive loss of basophilia of hepatic cells with dispersal of intracellular granules (mitochondria). 51

4) Hazard to wild life:

a) Although rotenone, derris, etc. are highly toxic to fish they are not looked upon as serious water pollutants; 75% of the toxicity is lost, it is reported, in 34 days. Nonetheless, a small lake is said to have remained toxic for 1 month, with deleterious effects toward fish, at a 0.066 ppm rotenone content. A variety of “fish-food-organisms” such as insects, crustacea and snails is reported not to be affected at 0.005 ppm rotenone. 1972, 2899

b) For birds (wild) toxicity for nestlings is relatively high, older birds being much more resistant. It is reported that 10 cabbage worms heavily dusted with derris powder are lethal to young American robins (nestling birds) and that 65 such caterpillars are lethal to young pheasants of various species. Ground derris is stated to be 25 times as toxic for birds as the pure rotenone (0.75%) it contains. 673

c) The residue hazard of most formulations is slight.

5) Phytotoxicity:

a) Non-phytotoxic; no hazard for plants (due attention must be paid to other elements of rotenone-containing formulations such as solvents, carriers, etc. which may themselves have a phytotoxic hazard. 129, 2120,353

6) Miscellaneous: Toxicity of various species of the genus Tephrosia (= Cracca) for Carrassius auratus (goldfish); acetone extracts concentration = 1 cc extract from 0.2 g of plant per 1000 cc H_2O:

6) Miscellaneous (Continued)

Plant	Part	Average Time Of Death (In Minutes)	Plant	Part	Average Time Of Death (In Minutes)
Tephrosia piscatoria	aerial	179	Tephrosia virginiana	aerial	208
Tephrosia purpurea	stems	slight distress	"	roots	166
"	leaves	"	Tephrosia vogeli	seed pods	161
Tephrosia toxicaria	aerial	142	"	aerial	106
Tephrosia virginiana	stems	no effect in 7 hrs	*Derris elliptica	roots	92
"	leaves	207			

*Known rotenone content 1.7%.

7) Toxicity for insects:

a) Toxicity of Derris resins (rotenone dosage = 25% of given dose) for several insect species as determined by one investigator: 2219

Insect	Route	Dosage (μg/g) To Yield Given % Mortality									
		0%			50%			100%			
		♂	♂♀	♀	♂	♂♀	♀	♂	♂♀	♀	
Anasa tristis (adult)	Topical		>2.6 mg/g			-			-		
Anasa tristis (")	Injection		4.0			10.0			25.0		
Bombyx mori (larva)	Topical		-			-			<0.7		
Ceratomia catalpae (larva)	Topical		1.0			2.0			5.0		
Ceratomia catalpae (")	Injection		1.0			4.0			6.0		
Oncopeltus fasciatus (adult)	Topical		5.0			25.0			60.0		
Oncopeltus fasciatus (")	Topical	8.8*		7.2*		-			-		2822
Periplaneta americana (adult)	Topical	>2mg/g		>2mg/g		-			-		
Periplaneta americana (")	Oral	>1mg/g		>1mg/g		-			-		
Periplaneta americana (")	Injection	3.0	-	5.0	5.0	-	8.0	9.0	-	13.0	
Popillia japonica	Topical		5.0			25.0			60.0		
Popillia japonica	Injection		10.0			40.0			110.0		
Tenebrio molitor	Topical		5.0			19.0			75.0		

* = total extractives

b) Quantitative toxicity data of various investigators:

Insect	Route	Dose	Dosage	Remarks	
Aceratogallia sanguinolenta (adult)	Dipping	LC_{50} (ca.)	1.653 g/100cc	As derris susp. 5.8% rotenone; 30 seconds exposure.	3239
Anasa tristis (adult)	inj	LD_{50}	10 μg/g	As derris resin, 25% rotenone.	2219
Anasa tristis (")	Topical	LD_{50}	>2600 μg/g	" "	2219
Aphis rumicis	Topical	LC	0.0005%	As a suspension in water.	712
Anopheles quadrimaculatus (4th instar)	Medium	MLC_{100}	10 ppm	60% kill at 1 ppm.	2020
Apis mellifera	or	LD_{50}	3 μg/g	As a suspension in water.	297
Bombyx mori (larva)	Topical	LD_{100}	<0.7 μg/g	As derris resins, 25% rotenone.	2219
Bombyx mori (4th instar)	or	LD_{50}	3 μg/g		2818,1743
Bombyx mori (5th instar)	inj	LD_{50}	7 - 10 μg/g	As emulsion in water of an oil solution.	846
Ceratomia catalpae (larva)	Topical	LD_{50}	2 μg/g	As derris resins, 25% rotenone.	2219
Ceratomia catalpae (")	inj	LD_{50}	4 μg/g	" "	2219
Chaoborus astictopus (winter larva)	Medium	LC_{98}	1.0 ppm	Derris powder, 5% rotenone.	768
Chaoborus astictopus (")	Medium	LC_{97}	0.5 ppm	" "	768
Chironomus spp (larva)	Medium	MLC	1.0 ppm	Exposure 1 hour.	1972
Chironomus spp (larva)	Medium	LC_{100}	6.0 ppm	In 46 - 52 hours' exposure.	979
Chironomus spp (")	Medium	LC_{65}	3.0 ppm	As Derris powder, 5% rotenone.	979
Culex pipiens (larva)	Medium	LT_{50}	1:100,000	151 minutes LT_{50} = Time for 50% kill at given conc.	458
Culex quinquefasciatus (larva)	Medium	LT_{50}	1:200,000	272 minutes	458
Culex territans (larva)					458
Heliothis armigera (larva)	or	LD_{50}	>490 μg/g		1381
Melanoplus differentialis	or	LD_{50}	>2000 μg/g		2610
Melanoplus femur-rubrum	or	LD_{50}	4700-7000 μg/g		2610
Lygus atriflavus (nymphs)	Topical	$LDeposit_{35}$	>50.5mg/100cm^2	As cubé dust.	1010
Lygus elissus (adult)		$LDeposit_{55}$	12.0mg/100cm^2		
Lygus hesperus (adult)		$LDeposit_{100}$	ca. 50.5mg/100cm^2		
Musca domestica (adult)	Contact Spray	LC_{50} 72hrs	0.3 mg/cc	In acetone.	3006
Musca domestica (")	Contact Spray	LC_{50} 72hrs	0.3 mg/cc	In kerosene-cyclohexanone 9:1.	3006
Oncopeltus fasciatus (adult)	Topical	LD_{50}	25 μg/g	As derris resins, 25% rotenone.	2219
Periplaneta americana	Topical	LD_{50}	>2000 μg/g	" "	2219
Periplaneta americana	or	LD_{50}	>1000 μg/g	" "	2219
Periplaneta americana	inj	LD_{50}	♂5.0, ♀8.0μg/g	" "	2219

b) Quantitative toxicity data of various investigators (Continued)

Insect	Route	Dose	Dosage	Remarks	
Periplaneta americana	inj	LD_{50}	6 - 15 $\mu g/g$	Water emulsion of oil solution.	846
Popillia japonica	Topical	LD_{50}	25 $\mu g/g$	As derris resins, 25% rotenone.	2219
Popillia japonica	inj	LD_{50}	40 $\mu g/g$	" "	2219
Vanessa (= Cynthia) cardui (larva)	or	LD_{50}	30(21 - 72) $\mu g/g$		1381
Leptinotarsa decemlineata (5th instar)	or	LD_{50}	0.2 $\mu g/g$		2610
Datana ministra	or	LD_{50}	110(70 - 180) $\mu g/g$	As dihydrorotenone.	1381

c) Rotenone, related rotenoids, derivatives; toxicity for insects: [2818, 712, 3006, 3059, 2131]

Compound	Bombyx mori (4th instar) LD_{50}, oral ($\mu g/g$)	Musca domestica LC_{50} 72 Hrs (mg/cc) In Acetone	Musca domestica LC_{50} 72 Hrs (mg/cc) Kerosene + In Cyclohexanone 9:1	Aphis rumicis LC(%) Suspension	Relative Toxicity At LC_{50} Aphis rumicis	Relative Toxicity At LC_{50} Macrosiphoniella sanborni
Rotenone	3	0.3	0.3	0.0005	1 = standard	1
Dihydrorotenone	<10	-	-	-	-	-
l-Dihydrorotenone	-	0.43	0.38	-	-	-
l-β-Dihydrorotenone	-	0.71	0.52	-	-	-
Dehydrorotenone	>400	-	-	-	-	-
Deguelin	10 - 12	2.8	0.59	0.005	-	-
l-Deguelin	-	0.6	0.57	-	-	-
Dihydrodeguelin	-	10	0.83	-	-	-
l-Dihydrodeguelin	-	0.57	0.51	-	-	-
Tephrosin	30 - 60	-	-	0.02	-	-
Toxicarol	>1540	-	-	0.2	-	-
Rotenol	> 510	-	-	-	-	-
Tubaic acid	> 540	-	-	-	-	-
l-α-Toxicarol	-	-	-	-	15	6
Sumatrol	-	-	-	-	13.1	-
l-Elliptone	-	-	-	-	-	5
Derritol	>870	-	-	-	-	-

N.B. Consider the importance of optical activity and solvent in rotenone toxicity.

d) Toxicity for Musca domestica of non-crystalline constituents of Tephrosia virginiana root; used as contact sprays in two solvents: 1219

Material	Concentration (mg/cc)	% Mortality After 72 Hrs Applied In Kerosene-Cyclohexanone 19:1	% Mortality After 72 Hrs Applied In Acetone
Rotenone	0.125	38	27
Rotenone	0.25	65	48
Rotenone	0.5	85	72
Neutral Resin	0.5	11	11
Neutral Resin	1.0	26	34
Neutral Resin	2.0	66	74
Alkali Soluble Fraction	0.5	5	5
Alkali Soluble Fraction	1.0	10	4
Alkali Soluble Fraction	2.0	7	8
Oil	0.5	7	2
Oil	1.0	7	3
Oil	2.0	8	9
$C_{21}H_{22}O_4$	2.0	-	4
$C_{22}H_{24}O_4$	2.0	-	4
Solvent (control)	-	8	3

e) Rotenone and Derris root acetone extract vs. Apis mellifera, Aphis pomi, and Aphis sorbi as contact insecticides; comparison with acetone extracts of pyrethrum flowers (0.9% pyrethrins): 1181

Substance Rotenone* g: cc H_2O	Apis mellifera % Mortality 24 Hrs	Aphis pomi and Aphis sorbi % Mortality 24 Hrs
1:2500	100	-
1:5000	74.5	-
1:10,000	66.8	93.4
1:20,000	26.7	80.6
1:40,000	19.1	76.3
1:80,000	6.4	93.4
1:160,000	-	83.2
1% acetone control	2.0	-
0.5% acetone control	0.0	15.5
H_2O control	2.4	11.7

e) Rotenone and Derris root acetone extract vs. Apis mellifera, Aphis pomi, and Aphis sorbi as contact insecticides (Continued)

Substance		Apis mellifera % Mortality 24 Hrs	Aphis pomi and Aphis sorbi % Mortality 24 Hrs
Derris root**g: cc H_2O	Approximate Dilution Rotenone		
1:400	1:13,200	100	93.0
1:800	1:26,400	69.6	82.1
1:1600	1:52,800	9.7	77.1
1:3200	1:105,600	3.4	73.0

*From stock solution of 1 g per 100 cc acetone.
**Rotenone content of root was ca. 3%.

Pyrethrum g flowers:ccH_2O	Approximate Dilution Pyrethrins		
1:400	1:44,000	89.3	52.0
1:800	1:88,000	84.5	46.2
1:1600	1:176,000	50.0	38.4
1:3200	1:352,000	44.7	43.1

f) Cubé dusts + various oils formulated with talc to give dusts of 0.25% rotenone content vs. aphids at 70°F, R.H. 50%, exposure 2 days. Cubé dust rotenone content = 4.2%: 1612

Material	LC_{50} ($\mu g/mm^2$) For	
	Myzus persicae	Aphis gossypii
Rotenone 0.25%	2.68	1.76 ± .5
" + peanut oil 1%	1.45 ± .29	1.23 ± .23
" + grapefruit seed oil 1%	1.45 ± .17	0.96 ± .20
" + soybean oil 1%	1.48 ± .21	0.85 ± .09
" + olive oil 1%	1.52 ± .17	1.18 ± .16
" + sodium oleyl sulfate 1%	2.41 ± .49	1.62 ± .32
" + peanut oil 1% + sodium oleyl sulfate 1%, H_2O 1%	2.12 ± .86	1.19 ± .14
Nicotine 0.67%	2.8	4.91
" 1.33%	-	4.29
Rotenone 0.33%, tobacco dust 16.67%, sulfur 16.67%	2.66	-

(1) Toxicity of rotenone and derris for Anasa tristis and Oncopeltus fasciatus is increased by tung, teaseed, corn, peanut, olive, soybean and linseed oils. 1081

(2) Toxicity of rotenone and derris for Macrosiphum pisi is enhanced by cottonseed, castor, peanut, coconut and neat's foot oils. 798,1257 344

(3) Soybean oil enhances rotenone and derris toxicity for Galerucella xanthomelaena. 1106

g) Relative resistance and susceptibility of various insects exposed to rotenone sprays or dusts (sprays in turkey red oil; dusts in talc) deposited at 0.38 $\mu g/cm^2$: 3109

Insect	% Mortality With Rotenone At 0.38 $\mu g/cm^2$ In	
	Spray	Dust
Myzus persicae	0	--
Bombyx mori	98	100
Agelastica alni	95	80
Vanessa polychloros	30	10
Euproctis chrysorrhoea	15	0
Athalia spinarum	10	--
Dendrolimus pini	4	8
Vanessa io	0	0
Vanessa urticae	0	--
Smerinthus ocellatus	0	0
Agrotis spp.	0	0
Lymantria monacha	0	--
Stilpnotia salicis	0	0
Carpocapsa pomonella	0	0
Oryctes nasicornis	0	--
Melolontha spp.	0	--

h) Relative toxicity of rotenone and rotenoids for Macrosiphoniella sanborni: 499

Rotenone = 1
Deguelin = 1/5
Sumatrol = 1/15
Elliptone = 1/5
Malaccol = ?
Toxicarol = 1/6

i) Rotenone vs. *Oryzaephilus surinamensis* (adult), *Aphis rumicis* and *Macrosiphoniella sanborni* (adult parthenogenetic viviparous ♀♀); medium: 5% saponin in water + 10% ethanol with pure crystallized rotenone: 2531

O. surinamensis (Temp. 61°F, R.H. 52%)		*A. rumicis*		*M. sanborni* (Temp. 65°F R.H. 75%)	
Conc. mg/l	% Kill	Conc. mg/l	% Kill	Conc. mg/l	% Kill
(Av. Deposit 4.89 mg/cm²)		(Av. Deposit 5.14 mg/cm²)		(Av. Deposit 5.47 mg/cm²)	
9.9	3.1	6	13.1	2	2.2
21.0	3.0	8	29.8	4	32.0
30.9	11.4	9	21.3	6	58.0
40.8	32.3	10	37.4	8	63.3
51.9	60.0	11	45.9	10	77.6
61.8	86.1	12	42.1	12	90.0
Control	3.5	14	58.4	14	93.8
--	--	16	58.7	16	100
--	--	18	70.8	Control	2.04
--	--	20	80.9	--	--
--	--	Control	4.08	--	--

j) Effectiveness of rotenone insecticides vs. various insect species; laboratory tests; cubé = *Lonchocarpus utilis*, timbo = *Lonchocarpus urucu*. D = *Derris*, T = *Tephrosia*, t = timbo, c = cubé. 109

Insect	Method Of Application	Order Of Effectiveness
Ceratomia catalpae	Leaf sandwich	D,T >t, >c
Epilachna varivestis	Dust on food	D,T >t >c
Rhopalosiphum pseudobrassicae	On insect and on food	D,T >t >t
Leptinotarsa decemlineata	On insect and on food	D > T > t > c
Brevicoryne brassicae	On insect and on food	D, T >t
Murgantia histrionica	On insect	D,T = or > t > c
Nezara viridula	On insect	D low effectiveness
Anticarsia gemmatilis	On insect, also residues	D, c, t ineffective
Feltia annexa	Insect in contact	D,T ineffective
Apantesis phyllira	Insect dusted	D,T,t,c low effectiveness
Anasa tristis	Insect coated	D = c = t
Chrysocus auritus	"	D > c
Evergestis rimosalis	"	D > c
Autographa brassicae	"	D > c

k) Derris constituents as contact insecticides: 712,711

Insect	Plant	Concentration (g/cc)	Net Mortality % With (Laboratory tests) Rotenone	Deguelin	Tephrosin	Toxicarol
Aphis rumicis	*Nasturtium*	1:500	--	--	--	94.5
"	"	1:5000	--	--	100	--
"	"	1:10,000	--	100	--	0
"	"	1:20,000	--	100	65	0
"	"	1:30,000	--	99	--	--
"	"	1:200,000	100	--	--	--
Brevia brassicae	Cabbage	1:500	--	--	--	0
"	"	1:5000	--	94	0	0
"	"	1:10,000	--	95.1	--	--
"	"	1:20,000	--	--	0	--
"	"	1:30,000	--	66.4	--	--
"	"	1:100,000	100	--	--	--
Trialeurodes vaporariorum (larva)	Bean	1:500	--	--	--	25.0
" "	"	1:2000	--	19.7	--	--
" "	"	1:5000	--	25.0	0	ca. 5
" "	"	1:20,000	--	34.0	14.0	ca. 5
" "	"	1:30,000	94.9	23.0	--	--
Thrips tabaci	Bean	1:250	--	--	--	12
"	"	1:2000	--	>50	--	--
"	"	1:10,000	--	>50	--	0
"	"	1:20,000	94.2	--	--	--
Tetranychus telarius	--	1:2000	60.7	ca. 10	--	18
"	--	1:5000	--	ca. 10	ca. 10	12
"	--	1:20,000	18.5	--	ca. 10	10

Greenhouse tests (Dust In Diatomaceous Earth)

Insect	Plant	Net Mortality % With 1% Rotenone
Aphis rumicis	Nasturtium	100
Myzus persicae	Cabbage	76.6
Aphis gossypii	Celery	68.9
Pseudococcus citri	Coleus	0
Thrips tabaci	Bean	65.5
Tetranychus telarius	Bean	0

Field tests (Dust in Diatomaceous Earth)

Insect	Plant	Net Mortality % With 1% Rotenone	2% Rotenone
Aphis pomi	Apple	77.2	
Illinoia liriodendri	Tuliptree		88.4
Anasa tristis (nymph)	Squash	< 50	< 50
Pontia vapae (larva)	Cabbage	100	100
Epilachna corrupta	Bean	100	
Blattella germanica	Cage tests	99	100 within 24 hrs
Menopon pallidum	Chicken lice	100	100
Menopon stramineum	"	100	100

1) Contact insecticidal action of rotenone toward various insects when applied as a suspension of pure rotenone (recrystallized from alcohol, m.p. 163°C) in water. 711

Greenhouse trials:

Insect	Plant	Concentration (g/cc)	Mortality %
Aphis rumicis	Nasturtium	1:100,000	99.5
"	"	1:200,000	100
"	"	1:300,000	97.0
Brevicoryne brassicae	Cabbage	1:100,000	100
"	"	1:200,000	97.4
Myzus persicae	Cabbage	1:100,000	98.2
"	"	1:200,000	94.3
Pseudococcus citri	*Coleus*	1:250	25
Trialeurodes vaporariorum (eggs)	Bean	1:2000	99.1
" "	"	1:20,000	82
" "	"	1:100,000	9.6
Trialeurodes vaporariorum (larva)	Bean	1:30,000	94.9
" "	"	1:60,000	88.8
" "	"	1:100,000	94.7
Thrips tabaci (adult, larva)	Bean, etc.	1:20,000	94.2
" "	"	1:30,000	69.3
" "	"	1:100,000	0
Blattella germanica	(Caged insects)	1:250	0 dipped 30 seconds
"	(")	1:2000	10
"	(")	1:10,000	10
Malacosoma americana (3rd instar)	Plum, Apple Trees	1:100,000	47.0
" (2nd ")	"	1:30,000	100
Tetranychus telarius		1:90	78.6
"		1:1000	64.5
"		1:2000	60.7
"		1:20,000	18.5
Field Tests:			
Anuraphis rosae	Apple	1:40,000	96.3
"	"	1:60,000	90.2
Aphis persicae-niger	Peach	1:40,000	98.3
Aphis pomi	Apple	1:60,000	99.0
Adelges (eggs)	Pine	1:20,000	0
Typhlociba comes (nymphs)	Grape	1:100,000	100
Anasa tristis (adults, nymphs)	Squash	1:250	10
" (")	"	1:500	5
Thrips sp.	*Plantago*	1:10,000	100
"	"	1:20,000	39
Diabrotica duodecempunctata (adult)	Potato	1:20,000	0
Doryphora decemlineata (adult)	"	1:2000	60
" (")	"	1:5000	12
" (eggs)	"	1:10,000	0
" (small larvae)	"	1:30,000	100
" (large ")	"	1:30,000	95
Epilachna corrupta (adult)	Bean	1:10,000	96.5
" "	"	1:5000	100
" "	"	1:10,000	85
" "	"	1:20,000	0
" (small larvae)	Bean	1:60,000	93.3
Popillia japonica (adult)	*Polygonum*	1:1000	100
" (")	Leaves in Cage	1:5000	97.3
" (")	"	1:7500	88.8
" (")	"	1:10,000	85.8

1) Contact insecticidal action of rotenone toward various insects when applied as a suspension of pure rotenone in water (Continued)

Field Tests (Continued)

Insect	Plant	Concentration (g/cc)	Mortality %
Popillia japonica (adult)	Leaves in Cage	1:15,000	86.1
" "	"	1:20,000	60.9
Culex (larvae)	Medium	1:1,150,000	98 - 99
" (")	"	1:2,300,000	95

8) Comparative toxicity, rotenone and other compounds vs. insects:

a) Speed of toxic action of various insecticides for Macrosiphum pisi on young Vicia faba plants, using dusts (in talc) applied in a dusting tower: 520

Insecticide	Concentration (%)	Temperature (°F)	Time To Yield			
			50% Kill		98% Kill	
			Hrs	Min	Hrs	Min
Nicotine	3	72	0	12	0	50
"	1	72	0	15	1	12
TEPP	0.18	74	0	20	0	56
Rotenone (5% rotenone, 10% other extractives)	5	72	0	47	1	23
Lindane	1	72	0	56	1	54
DDT	5	72	0	57	1	45
Parathion	2	70	1	21	1	53
"	1	70	1	8	1	43
Methoxychlor	10	75	2	1	5	34
DDD	5	72	2	34	4	35
Aldrin	1	75	3	44	7	32
Dieldrin	1	75	4	7	6	43
EPN	0.86	74	5	26	8	6
Chlordane	5	72	9	24	18	8
Toxaphene®	5	72	13	20	19	1
Talc	100	67 - 72	13	28	23	51

b) Comparative toxicity, Derris (25% rotenone) resins and other compounds for several insect species: 2219

Insect	Route	Amount (μg/g) To Produce % Mortality Indicated With									
		Derris		Pyrethrins		Lethane 384		Sodium arsenate		Nicotine	
		50%	100%	50%	100%	50%	100%	50%	100%	50%	100%
Anasa tristis	Topical	≫2600	≫2600	7	26	-	-	-	-	350	1250
"	Injection	10	25	10	25	-	-	20	40	200	350
Bombyx mori (larva)	Topical		<0.7		<0.4	-	-	-	-	4	8
Ceratomia catalpae (larva)	Topical	2	5	2	6	-	-	-	-	100	200
"	Injection	4	6	4	6	-	-	20	30	80	150
Oncopeltus fasciatus	Topical	25	60	8	28	400	750			190	450
Periplaneta americana	Topical	≫2000	≫2000	6.5	12	960	2300	250	1300	650	1300
"	Injection	7	13	6	11	170	400	45	70	100	200
Popillia japonica	Topical	25	60	40	130	800	1700	850	1700	650	1000
"	Injection	40	110	40	110	30	90	50	100	400	900
Tenebrio molitor	Topical	19	75	35	100	850	1600	-	-	3200	4400

9) Pharmacological, pharmacodynamic, physiological, etc., insects:

a) The action by which rotenone kills insects remains essentially unknown. 151

(1) The heart action is slowed and the breathing rate, but these phenomena are too protean to situate properly the site of action of rotenone in the tissues.

b) Rotenone acts both as a stomach and/or a contact poison; entry to the insect body may be: 1) Directly through the integument; 2) by extraction on the part of external body fluids and exudates; 3) via the spiracles, tracheae, and alimentary tract. 3094 3251

(1) Entry to the tick Melophagus ovinus is chiefly via the spiracles. Susceptibility is decreased by sealing the spiracles and enhanced by accelerating the breathing rate. Temperature rise by 10° decreases killing time by more than ½ (13 hrs vs. 5.5 hrs). The integument is entered directly at 30°C but not at 20°C.

(2) Use of abrasives (alumina), detergents and solvents on the cuticular waxes (lipids) of Rhodnius speeds rotenone action. 3298 3300,3252

Effect of solvent on penetration of rotenone into Melophagus ovinus:

Solvent	Time For Death (Hrs)	Solubility Of Rotenone In g/100 cc At 30°C	
		In Solvent	in 20% Saturated Solvent + Water
Ortho-Cresol	2	48	0.4
Xylenol	2	62	0.75
Benzyl alcohol	2	21	0.5
4 Methyl cyclohexanol	3	1.0	0.2
Carbitol	7	2.7	0.75
Methyl benzoate	6	18	<0.1
Rotenone (alone)	6	--	--

(3) High efficiency of solvent is correlated with high rate of penetration through bees wax, high partition coefficient between wax and water, and high solubility of insecticide in a water solution of the solvent. 3252 409

(4) The arthropod body may show a localized susceptibility to penetration by rotenone, for instance Ixodes ricinus is particularly susceptible on the tarsi; on dorsum, pure rotenone intoxicates in an average of 4 days, on tarsi in 4 hours. 0.1% rotenone in olive oil acts more rapidly than 0.1% in castor oil, although rotenone is more soluble in the latter. Vs. Ornithodoros moubata petroleum oil solutions are more effective than vegetable oil solutions.

c) Physiological signs of rotenone action:

(1) Bombyx mori (larva): Regular beat of heart for 30 minutes, then rapid decline in rate during ca. 10 minutes followed by great irregularity of rate and amplitude with occasional halts succeeded by a 2nd rapid decline for ca. 10 minutes, then a long period of feeble and irregular action until death. Thus, three phases: Hyperactivity, incoordination, prostration and quiescence. 3094

(2) Injection into the metathoracic trochanter of Melanoplus: Almost immediate halt of respiratory movements, decrease in O_2 consumption to 42% of normal. Rotenone depressed the O_2 uptake of Oryzaephilus surinamensis adults. (DDT, lindane, pyrethrins, DNOC stimulated O_2 uptake.) 3094 2041

(3) Periplaneta americana: At 1×10^{-8} M rotenone brought on a decline in amplitude of the diastolic contraction of the heart; frequency of pulsation was slowed, with a halt in diastole, within 20 minutes after rotenone injection at 100 μg/g. 1861 2421

(4) At 100 μg/g application to Blattella germanica: Slight increase in respiratory rate; after 100 minutes a long decline to flaccid paralysis and death. 1441

(5) Rotenone fed to Prodenia eridania (6th instar): Feces highly toxic to mosquito larvae (no detoxification of rotenone, no absorption via gut). 86% of fed rotenone recovered. Prodenia eridania tissues did not detoxify rotenone in 18 hrs. incubation. No histological abnormalities noted in gut of Prodenia fed 5 mg of crystalline rotenone. 3347 3349

(6) No specific effects of rotenone could be detected on nerve-muscle preparations. 3094

(7) No effect of rotenone on flow of nerve impulses in central nerve cord of Porthetria dispar (larva). 1822

(8) No histopathological effects in nerve tissues of rotenone-poisoned Melanoplus, or Tenebrio; vs. Musca 0.00625% rotenone sprays were lethal sans "knockdown" but produced no demonstrable nerve lesions; a 0.25% spray yielding 94.7 "knockdown" in 10 minutes gave dissolution of brain fiber tracts and vacuolization of neuron body within 10 minutes of treatment. 1420

(9) In Thermobia domestica, recovering from sub-lethal doses, appendages were sloughed many weeks after exposure. 3028

(10) In in vitro preparations of Periplaneta americana coxal muscle cytochrome oxidase rotenone at 10^{-5} M stimulated, as measured by O_2 uptake in Warburg's apparatus; no stimulation at 10^{-3} M. 2305

d) Detoxification of rotenone in light: 1723

Material	Loss Of Toxicity (%) When Exposed to Sunlight For				Loss Of Toxicity (%) When Exposed To Arc-Light For			
	10 Days		20 Days		240 hrs		480 hrs	
	Insect Test	Fish Test	Insect Test	Fish Test	Insect Test	Fish Test	Insect Test	Fish Test
Rotenone	64	80	73	79	94	98	98	99
Dihydrorotenone	32	25	73	75	ca. 100	98	ca. 100	ca. 100
Rotenone HCl	71	76	86	78	98	99	98	99
Rotenone-Bentonite	77	76	86	83	ca. 100	90	-	-
Rotenone-lampblack	37	49	29	51	67	87	-	-
Derris root	75	41	91	73	ca. 100	92	-	-
Derris extract	89	86	93	86	ca. 100	97	-	-

e) Particle size and rotenone toxicity: 2195,2196,2197

(1) Rotenone in 5 types of suspension, viz. colloidal, as small elongated plates, as small hexagonal plate aggregates, as 2 suspensions of hexagonal plates of different size: Tested by dipping Oryzaephilus surinamensis and Tribolium castaneum: Within range of crystal size to 150 micra toxicity is inversely related to particle size (opposite effect in case of DDT); variation of LC_{50} of order of 600 times; crystal shape is unimportant; similar effects from fine suspensions by spray methods. Colloidal rotenone gives initial paralysis followed by recovery.

(2) Rotenone by topical application to Oncopeltus fasciatus (adult): Colloidal form more toxic than a crystalline suspension.

(3) By injection into O. fasciatus rotenone crystal suspensions proved equal in toxicity to colloidal suspensions at 27° C for 2 days post-treatment; at 10°C colloidal rotenone was greatly more toxic than the crystalline form 2 days post-treatment; if insects are maintained 3 weeks and inspected at intervals the apparent difference in toxicity grows less and less and in the end almost disappears. In topical application the toxicity difference between colloidal and crystalline suspensions is real and does not disappear with time. The difference in toxicity on injection is a difference in speed of action, not in ultimate toxicity.

(4) Vs. Oryzaephilus surinamensis rotenone colloidal suspensions were greatly more toxic than crystalline suspensions. In contact action the toxicity of small particles is enhanced by cooling the insects after treatment. By injection, particle size has no influence on toxicity if insects are kept warm after treatment. In cool-kept insects colloid acts more rapidly than crystals, but ultimate kills from each are the same. In contact action small particles have a solubility advantage.

10) Rotenone and beneficial insects:

a) As Derris ground root (5% rotenone content) at 1½ lbs per 50 gallons water (spray) vs. Hippodamia convergens (adult) by 5 application methods: Method I average kill = 71% (67 - 74%); II = 98 - 99% kill; III = 57% kill (37 - 71%); IV = 72% kill (68 - 86%); V = 73 - 78% kills; eggs: Average kill = 14% (0 - 25%); larvae (1st instar): Average kill = 46% (43 - 48%). Hazard to some beneficial forms is evidently great. 1450

11) Refractoriness of some insects to rotenone:

a) Diataraxia oleracea (larva, final instar) is reported to have survived oral doses of pure rotenone at 200 μg/larva. 3245

158

RYANIA, Active Principle = RYANODINE

Tentative empirical formula for ryanodine = $C_{25}H_{35}NO_9$ or $C_{26}H_{37}NO_9$.

GENERAL [Refs.: 1464, 481, 3159, 353, 2231, 2120, 129, 2689, 1768, 2565, 1878]

Ryania as the insecticide is the ground stem-wood (or its extracts [active principle: The alkaloid ryanodine]) of Ryania speciosa, a genus of small shrubs and trees belonging to the family Flacourtaceae and native to tropical America. Ryania speciosa occurs on the island of Trinidad; other species of the genus occur elsewhere in tropical America. The active principle is present in stem-wood and roots, with the greater amount in the latter. For reasons of conservation, regrowth, etc., the stem-wood is used, though the amount of insecticidal substance is less than in the roots. Ryania is toxic to a wide variety of insects and presents little hazard to man and none to plants. The active principle is water soluble but of high stability in storage and on exposure to light. Ryania has become, since the discovery of its insect toxicant properties in 1945, widely recognized for its value in control of the European corn borer against which it is equally toxic or more toxic and effective than DDT. Ryania is reported to be superior to cryolite for sugar-cane borer, doing no harm to the crop nor bringing about an increase in aphid infestation. It is highly toxic for oriental fruit moth, squash borer, cabbage caterpillars, coddling moth, cotton bollworm, southern green stink bug, soybean caterpillars and corn earworm. Ryania acts as a selective, fast-acting stomach poison. Toxic to the insects above mentioned, Ryania is ineffective vs. sweet potato weevil, cabbage maggot, cauliflower worms, Japanese beetle larvae, boll weevil, cotton aphid and plum curculio. Ryania produces (in susceptible insects) a quick cessation of normal activity, notably feeding, although death may not ensue for several days. Toxicity is not confined to stomach action, Ryania being toxic to insects by contact also. Reports have appeared of systemic activity via the juices or tissues of treated plants.

PHYSICAL, CHEMICAL (Physical properties given apply to ryanodine.) [Refs.: 2689, 1768, 2231, 129, 2120]

The active principle of Ryania wood or roots, the alkaloid ryanodine, is extractable with water, methanol, chloroform, and may be isolated as a colorless, crystalline solid; m.p. (with decomposition) 219° - 220°C; neutral to litmus; not salt-forming; soluble in water, alcohol, acetone, ether, chloroform; insoluble in petroleum ether, benzene; distribution coefficient ether/water = 1.3; ultra-violet absorption spectrum maximum at 2685°Ångstrom in alcohol solution; oxidizable by periodic acid and lead tetraacetate to yield oxoryanodine ($C_{25}H_{33}NO_9$), m.p. 227°C; acid treatment yields anhydroryanodine ($C_{25}H_{33}NO_8$), m.p. 275°C; alkaline saponification yields pyrrole-α-carboxylic acid and $C_{20}H_{32}O_8$ m.p. 252°; not precipitated by the usual reagents for alkaloids; $[\alpha]_D^{25^\circ} = +26^\circ$; more stable than rotenone or pyrethrins to exposure in air or light. In stems and roots, ryanodine and chloroform-extractable substances = 0.16 - 0.2%.

a) Formulations: Ground stems as Ryanex®; (powdered stems and roots mixed with inert earths are more stable than extracts to ultra-violet light) usually formulated as 40% dusts.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) The active principle among the Ryania alkaloids, ryanodine, is very toxic to animals; 2 to 5 μg/g (2 to 5 mg/k) elicit symptoms in the frog and mouse. Ryania as ground stems is considered of low toxicity for higher animals. 2231 851

b) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	or	LD	1200	As powdered stems of Ryania speciosa.	1464,1878
Dog	or	LD	150	" "	1464,1878
Monkey	or	LD	>400	" "	1464,1878
Rabbit	or	LD	650	" "	1464,1878
Mouse	or	LD	650	" "	1464,1878
Guinea Pig	or	LD	2500	" "	1464,1878
Chicken	or	LD	>3000	" "	1464,1878
Rat	or	LD_{50}	ca. 750		1951
Rabbit	ct	LD_{50}	>4000		1952
Cattle	or	Minimum Toxic	1000	As a single oral dose.	2567

2) Chronic toxicity:

a) Rats, Guinea pigs and chickens have been maintained symptomless for at least 6 months on 1% of Ryania powder in the diet without any evidence of cumulative effect; no adverse effects on growth or food intake. 1464

b) Rats, fed Ryania powder at 5% of diet, showed decided losses of weight and some deaths within 25 days of the start of treatment. 1878

3) Pharmacological, pharmacodynamic, physiological, etc., higher animals:

a) Peculiar action on skeletal and cardiac muscle and on the CNS. Ryanodine alkaloid produces rigidity and contracture of muscle and cardiac failure. 851

(1) Some elements of the action disappear on nerve section.

b) In a dosage of 5 μg/g ryanodine given intraperitoneally in Rana pipiens induced quickly a flaccid paralysis, which passed into complete rigor.

c) Dilutions of ryanodine to 10^{-8} produced irreversible rigor in isolated Rana rectus abdominis muscle preparations. The perfusate was rendered active by contact with the treated muscle. At 10^{-4} direct application to exposed ganglia or nerves produced no effect on ganglionic or axonic transmission, sensory activity, or neuromuscular transmission.

d) Symptoms of poisoning include weakness, tremors, convulsions, coma and death.

4) Residue hazards:

a) Residues at 6 ppm on apples were found harmless to laboratory animals. 129

5) Hazard to wildlife:

a) Preliminary experiments on fish indicate "illness" in 14 - 24 hours in trout and bluegill; no effect on perch or goldfish. 129

6) Phytotoxicity:

a) Not phytotoxic.

7) Toxicity for insects:

a) Vs. Pyrausta nubilalis the alkaloid ryanodine proved ca. 700 times more toxic than the parent powdered stemwood of Ryania. 1464

b) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Blattella germanica ♀	Topical	LD_{50}	25 μg/g	As ryanodine; by measured drop method.	1464
Blattella germanica ♂	Topical	LD_{50}	5 μg/g	" ; " .	1464
Oncopeltus fasciatus ♀♂	Topical	LD_{50}	25 μg/g	" ; " .	1464
Aëdes aegyptii (larva)	Medium	LD_{50} 3 day	10 ppm	To yield 50% kill in 3 days.	1464

c) Qualitative:

(1) Toxic as a stomach and contact agent in the form of dusts, aqueous suspension sprays and crude extractives in water vs. Blattella germanica, Periplaneta americana, Aphis pomi, potato aphids, Anasa tristis, Oncopeltus fasciatus, Popillia japonica, Leptinotarsa duodecemlineata, Epilachna varivestis, Pieris rapae, Tenebrio molitor, Musca domestica, Bombyx mori, asparagus beetle, elm-leaf beetle, golden tortoise beetle, black carpet beetle, diamond back moth, cabbage looper, Pyrausta nubilalis, Heliothis armigera, Tineola bisselliella, sugar cane borer; not active against Thrips tabaci, mosquito larvae or European red mite. 1464

d) Pharmacological, pharmacodynamic, physiological, etc.; insects:

(1) Ryanodine by injection at 2 - 5 μg/g produced almost instant symptoms in Periplaneta americana, Blaberus cranifer, Platysymia cecropiae. 353

(2) 5 μg by injection in insects proved entirely depressant, bringing partial paralysis without response to stimuli; no central nervous system excitation or tremors were noted. 2231

(3) At 0.04 cc/g an extract of Ryania speciosa in water (1:10 w/w) applied to Periplaneta americana brought instant toxic reaction without recovery; in measured drop tests alcohol extracts were active vs. Blattella and Oncopeltus; petroleum ether extracts were inactive. 1464

(4) Intoxicated insects reveal a general depressant action; feeding, locomotion and reproduction come to a rapid halt, but the insect may persist in a semi-moribund state for a long time. 1464

(5) Sub-lethal doses in Periplaneta americana raised O_2 uptake to 9.6 times normal in 25 minutes at 5 μg/g, 4.2 times normal in 50 minutes at 0.5 μg/g, 2.3 times normal in 75 minutes at 0.05 μg/g (ryanodine). Peak of respiration was coincident with onset of paralysis, thereafter rapidly declining until death. Similar results could be elicited from other insects. 2231

(6) Using an injection combining ryanodine with adenosine triphosphate in Periplaneta, the interval to paralysis was shortened from 25 minutes (the interval with ryanodine alone) to 6 - 8 minutes; O_2 uptake was increased to 18 times the normal. Presumed is a specific action on the contractile mechanism of striated muscle and a postulated interference with the phosphagen-adenosine triphosphate-adenosine diphosphate-actomyosin cycle. 2231 1464

(7) A synergistic action is reported for Ryania with n-propyl isome, piperonyl cyclonene and sulfoxide. 353

e) Vs. Beneficial Insects:

(1) Vs. Apis mellifera Ryania is reported only slightly toxic on contact. 429

(2) Used in control of Carpocapsa pomonella Ryania proved harmless to natural predators and the red mite-predator balance, compared favorably with unsprayed plots indicating successful biological control. Results proved less favorable (Ryanex® used) on the braconid parasite Macrocentrus ancylovorus and other parasites of Grapholitha molesta, the oriental fruit moth. 2650

f) Field experiences in the economic control of insects:

(1) Blissus leucopterus was effectively controlled by Ryania in small grains. 248

(2) Vs. Tineola bisselliella deposits on wool at 0.0008% protected wool fabric. 1464

(3) Vs. Stored Products Insects in shelled corn: Insect "populations" were held to low levels by Ryania, ryania-sulfoxide, ryania-n-propyl isome dusts at 45 lbs per 1000 bushels corn; ryania-sulfoxide downgraded the product by an objectionable smell; residue was high after 7 months but variable. 81

(4) Vs. Pieris rapae, Trichoplusia ni: 30% dusts yielded more than 83% control. 796

(5) Vs. Anticarsia gemmatilis: Equal in effectiveness to DDT, BHC, cryolite. 110,1873

(6) Vs. Heliothis armigera: 40% dust was the most effective control. 1874

(7) Vs. Mineola vaccinii: Preferable to cryolite in control of. 229

(8) Vs. Pyrausta nubilalis: 50% dust at 35 lbs per acre were superior to nicotine or rotenone; 0.5% suspensions were effective for ground application. Reported by some to be unreliable in aircraft distributed sprays. 481 106

(9) Vs. Diatraea saccharalis: Equal to cryolite in highest effectiveness. 353

(10) Vs. Pectinophora gossypiella: Somewhat inferior to DDT. 2677

(11) Vs. Hylemyia antiqua, H. brassicae: Little toxicity for these insects. 796

(12) Vs. Galerucella xanthomelaena: Equal to DDT in effectiveness. 1107

159

SABADILLA (Cevadilla; Caustic barley; dried ripe seeds (or extracts thereof) of Schoenocaulon officinale = Sabadilla officinarum, = Asagraea officinalis.)

Also Veratrum viride, American false hellebore, which contains active principles similar to or identical with those of Schoenocaulon officinale.

GENERAL [Refs.: 353, 2231, 2120, 129, 1801, 39, 977, 784, 1859, 851, 1580, 40]

Although long employed by the autocthonous peoples of tropical America for control of body lice, Sabadilla has but recently attained a lively interest as an insecticide in the present day sense. Sabadilla has been taking its place among the insecticides of plant origin since the observation that alkali (or heat) treatment of the active principle bearing seeds of Schoenocaulon enhances the insecticidal potency of the product.

The active principle of Sabadilla is an alkaloid mixture of which the chief alkaloids are cevadine (= crystalline veratrine) and veratridine (= amorphous veratrine). Also present, in lesser quantity, are the alkaloids sabadinine, sabadine, sabadilline and sabatine. The whole alkaloidal complex is commonly called veratrine, or veratrine alkaloids. Present, in addition to the alkaloids, are sabadillic and veratric acids, fatty oils and resins. Schoenocaulon officinale, the source of sabadilla, belongs to the family Liliaceae. Also belonging to the family Liliaceae are Veratrum viride and Veratrum album, plants which contain in their roots insecticidally active alkaloids which are related to those of Schoenocaulon. Veratrum viride, for example, yields ca. 1.3% total alkaloids of which: Jervine = 17%; pseudo-jervine = 3.3%; germine = 1%; lesser amounts of rubijervine, isorubijervine, germerine, germidine, germitrine, veratrosine, veratrimine and protoveratridine are also present. These alkaloids are freed by alkali treatment and are chloroform-extractable.

Sabadilla seed has an alkaloid content of 2 - 4% of which cevadine ($C_{32}H_{49}NO_9$) = 13% and veratridine ($C_{36}H_{51}NO_{11}$) = 10% of the crude alkaloid complex.

Sabadilla is an important, selective contact insecticide, particularly for use vs. houseflies, household insects, chinch bugs, harlequin bugs, squash bugs, Lygus spp., lice, thrips and leaf-hoppers. Thus, the susceptible insects seem chiefly to group themselves among the Homoptera and Hemiptera. Purified cevadine, for example, is ca. 10 times more toxic than DDT for Musca domestica.

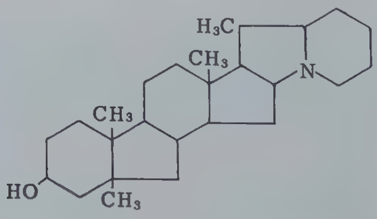
As for the alkaloids of Veratrum viride (which are costly, not standardized and limited in application to freshly ground roots if full effectiveness is to be had), these have found use in the control of chewing insects on ripening fruit because of the rapid loss of toxicity by the residues. The powdered roots, applied to horse dung, prevent the emergence of adult Musca domestica.

All the alkaloidal principles mentioned above are toxic to man. Principal insecticidal activity is considered to belong to cevadine and veratridine.

PHYSICAL, CHEMICAL N.B. The properties described are primarily for the veratrine mixture derived from sabadilla (= I) and for cevadine (veratrine) (= II). [Refs.: 1641, 353, 2231, 2120, 129, 1483, 8, 9, 39, 1064, 2801, 1065, 2773]

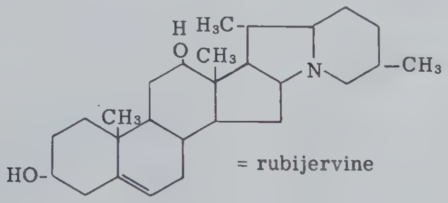
I: A white-gray powder; m.p. 145° - 155°C; soluble to 0.055 g/100 cc water (cold) and to 0.1 g/100 cc water at 100°C; 1 gram dissolves in 2.8 cc alcohol, 0.7 cc chloroform, 4.2 cc ether, 80 cc olive oil; 0.1 - 0.2 g dissolve in 100 cc kerosene; $[\alpha]_D^{17°} = +12.5°$ in alcohol; freely soluble in dilute acids, benzene and amyl alcohol; slightly soluble in glycerol; insoluble in petroleum ether.

II: A solid in colorless, prismatic crystals; m.p. (with decomposition) 205°C; slightly soluble in water (to 555 ppm); 1 gram dissolves in 15 cc alcohol or ether; on hydrolysis with alcoholic KOH, cevadine (veratrine) hydrolyses to cevine (= sabadinine) whose tentative ring system is:



Veratridine: m.p. 160° - 180°C. The insecticidal properties of ground seeds of Schoenocaulon officinale are greatly activated by heating the seeds to 75° - 80° for 4 hours, by wetting with 10% Na_2CO_3 or grinding with slaked lime; light quickly inactivates the sabadilla alkaloids.

Of the alkaloids of Veratrum viride only the structures of jervine and rubijervine (Δ^5 - solanidene - 3 - (β), 12-(α)-diol are known with any exactitude, although details are still in dispute.



= rubijervine

Veratrum Ester Alkaloids after Ref. 851.

Source	Ester	Alkamine (obtained on alkaline hydrolysis in alcohol)
	Protoveratrine A,B	Protoverine ($C_{27}H_{43}NO_9$)
Veratrum album	Germitrine	Germine ($C_{27}H_{43}NO_8$)
	Neogermitrine	Germine ($C_{27}H_{43}NO_8$)
Veratrum viride	Germidine	Germine ($C_{27}H_{43}NO_8$)
	Neogermidine	
Schoenocaulon officinale	Germerine	Germine ($C_{27}H_{43}NO_8$)
(Sabadilla)	Veratridine	Veracevine ($C_{27}H_{43}NO_8$)
	Cevadine	Veracevine ($C_{27}H_{43}NO_8$)

Veratrum viride and Veratrum album contain also the secondary amines veratramine and jervine which are piperidine derivatives. 851

Zygadenus venenosus: Another plant containing veratrum alkaloids of which three have been identified, the germine esters neogermitrine, germidine, neogermidine and two monoesters of zygadenine ($C_{27}H_{48}NO_7$), veratroyl zygadenine and vanilloyl zygadenine. The zygadenine esters resemble veratridine. 851

1) Formulations: As kerosene solutions; dusts 5 - 10% of ground seeds + lime carrier, dusts 10% - 20% + lime carrier.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) Powdered sabadilla seed is of relatively low toxicity for rats, being less toxic than DDT or rotenone; cevadine and veratridine account for the greater part of the toxicity, with cevadine being the more toxic of the two. 1859
   b) Some of the veratrine alkaloids have high pharmacological and pharmacodynamic action and may be in addition highly toxic, for instance cevadine. Germidine and germitrine (of Veratrum viride and V. album) have marked hypotensive activity. 851

Animal	Route	Dose	Dosage (mg/k)	Remarks	
As sabadilla (ground seeds):					
Rat	or	LD_{50}	ca. 4000		1951
Cevadine:					
Frog	sc	LD	15 - 30		1858
Frog	sc	LD	1.5		1858
Mouse	ip	LD_{50}	3.5 (2.7-4.4)		3036
Rabbit	sc	LD	0.5 - 1.3		1858
Cevine:					
Mouse	iv	LD_{50}	87		1857
Rat	ip	LD_{50}	67		1858
Veratrine:					
Mouse	ip	LD_{50}	8.5 (7.5-9.6)		3036
Mouse	ip	LD_{50}	7.5 (6.1-9.2)		3036
Veriloid: (A purified mixture of Veratrum viride alkaloids.)					
Mouse	ip	LD_{50}	3.2		204
Mouse	iv	LD_{50}	0.43		204
Rat	or	LD_{50}	12.2		2395
Rabbit	or	LD_{50}	18.7		204

1) Acute toxicity for higher animals (Continued)

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Veratridine:					
Mouse	iv	LD_{50}	0.42		1857
Mouse	ip	LD_{50}	1.35		3036
Rat	ip	LD_{50}	3.5		1858
Veratrone: (1 cc = 0.25 mg alkaloids. A semi-purified preparation of Veratrum viride.)					
Mouse	ip	LD_{50}	2.45 (1.8-3.2)		204
Protoveratrine A & B, Veralba: (Mixture of 2 alkaloids from Veratrum album.)					
Rana temporaria (Frog)	sc	LD_{50}	4.5		1324
Rana esculenta (")	sc	LD_{50}	13		1324
Mouse	iv	LD_{50}	0.048 (0.3-0.64)		1857
			(0.29-0.48)		
Mouse	ip	LD_{50}	0.44	From 2 different commercial sources.	3036
Mouse	ip	LD_{50}	0.37		3036
Rat	or	LD_{50}	5		1858
Rat	sc	LD_{50}	0.6		1858
Rabbit	sc	LD_{50}	0.11		1858
Rabbit	iv	LD_{50}	0.05		1324
Cat	sc	LD_{50}	0.5		1324
Protoverine (alkamine of protoveratrine ($C_{27}H_{43}NO_9$))					
Mouse	iv	LD_{50}	194		1857
Jervine					
Mouse	iv	LD_{50}	9.3		1857
Germine					
Mouse	iv	LD_{50}	139	Death in 13 minutes.	1857
Germidine					
Mouse	ip	LD_{50}	10 (9.1-11.0)		3036
Germerine					
Frog	sc	LD_{50}	9		1324
Frog	sc	LD_{50}	20		1324
Rat	or	LD_{50}	30		1858
Rat	sc	LD_{50}	3.7		1858
Rabbit	sc	LD_{100}	2		1324
Rabbit	iv	LD	0.3		1324
Cat	sc	LD	0.5		1324

(1) The toxic level of sabadilla seed (alkaloid ca. 2.5%; mainly cevadine and veratridine) in the diet of the rat = less than 2.5% of the ration (heat-treated seed). 1860

(2) The toxic level of sabadilla alkaloids in the rat diet = ca. 2.5%, (crude alkaloid mixture). This may be compared with 0.625% for DDT and rotenone, a level which brings death respectively in 3 - 5 and 7 - 9 days. 1860

2) Pharmacological, pharmacodynamic, physiological, etc., higher animals:

a) From the standpoint of therapeutic use of the veratrum alkaloids in man the range between therapeutic and toxic doses is narrow. 1221, 851

  (1) Side effects and toxic effects in the therapeutic range: Epigastric, substernal burning, unpleasant taste, salivation, sweating, hiccough, nausea, vomiting; effects more noticeable after oral than after parenteral administration.

  (2) Intravenous injections (protoveratrine, hypotensive dose) yield paresthesia of lips and tongue, warm sensation of face, mouth, throat, hands, feet, epigastrium and perineum, the warm sensation preceding blood pressure fall and enduring up to 25 minutes. No skin reddening but occasional face sweating and pressure sensation in epigastrium and under sternum unassociated with myocardial ischemia. 851

b) Veratrum alkaloids act mainly on the cardiovascular system, respiration, nerve fibers and skeletal muscle. The ester nature is important for the pharmacologic action—hydrolysis of the ester linkage abolishes some pharmacologic properties and markedly reduces others. 1221, 851

c) Cardiovascular effects: 1221,851

  (1) Reflex fall in blood pressure, reflex decrease in heart rate (Bezold effect).

    (a) Hypotensive action is due to peripheral vasodilation, purely reflex and afferent via the vagus fibers from left ventricle and lungs; efferent pathway undetermined; atropine prevents the hypotension in part only, the effect not being, thus, primarily cholinergic.

    (b) Veratrum alkaloids exert no direct vasodilator effect on blood vessels.

    (c) Veratrum alkaloids exhibit no ganglionic or adrenergic blocking action.

    (d) Hypotension and bradycardia are blocked by tetraethyl ammonium and may be overcome by sympathomimetic amines such as ephedrine and phenylephrine.

    (e) Bradycardia is reflex in nature, afferent and efferent pathways are vagal.

    (f) Large doses may decrease heart rate by direct central nervous action (central vagal stimulation?).

  (2) Some veratrum alkaloids may directly increase the force of contraction of the isolated mammalian heart without significant alteration of rate; large doses induce arrhythmias, ventricular tachycardia

and fibrillation. Veratramine and jervine exert a highly selective action on the pacemaker tissue and antagonize the cardio-accelerator effects of sympathomimetic amines.

(3) Renal hemodynamic effects:
  (a) The therapeutic veratrum alkaloids do not deleteriously affect renal function.
  (b) Hypotensive doses moderately decrease glomerular filtration; effective renal plasma flow is not altered or is but slightly decreased.
  (c) In excessive blood pressure fall leads to oliguria.
  (d) The reflex vasodilation includes the renal vessels, notably the glomerular arterioles.

(4) Cerebral circulation:
  (a) Decreases cerebrovascular resistance; blood flow, cerebral oxygen utilization or respiratory quotient are not altered.

d) Respiratory effects:
  (1) In greater than therapeutic doses brings respiratory depression.
  (2) Respiratory arrest is the main factor in lethal action of large doses on laboratory animals.
  (3) Small doses give reflex respiratory inhibition via vagal receptor ending stimulation in lungs; vagal section or block abolishes the action.
  (4) Direct central effect and direct bronchoconstrictor action in large doses; not mediated by vagus; non-cholinergic.
  (5) Therapeutic doses may depress respiratory rate and amplitude.

e) Neuromuscular effects:
  (1) Veratrine produces in skeletal muscle a prolonged secondary tetanus following the initial twitch induced by stimulus.
  (2) The above is accompanied by repetitive impulse discharge in muscle fibers.
  (3) In frog muscle at 10^{-5} - 10^{-7} concentration there occurs an increase in negative afterpotential following conduction of each muscle impulse along the fiber. Negative afterpotential associated with increased excitability and, if sufficiently great, trains of self-sustained high frequency after discharges may be produced leading to prolonged tetanus.
  (4) In high concentration, veratrine may elicit repetitive discharge from peripheral nerves as well as accentuation of negative afterpotential and slowing of repolarization after impulse passage. O_2 consumption, even at rest, is high under veratrinization.
  (5) Other excitable tissues, including cardiac and certain unstriated muscle types, may respond by electrical and mechanical changes as does skeletal muscle.
  (6) No direct effects are noted on synaptic transmission, myoneural junction or autonomic ganglia.
  (7) Burning sensation and sneezing, elicited by veratrum alkaloid contact, may reflect an action similar to that had on motor axons and muscle fibers.
  (8) Promotes potassium leakage from the cells of excitable tissues.

f) Absorption, excretion and metabolism:
  (1) Absorbed via gastrointestinal tract and subcutaneous tissues.
  (2) Oral dose must be 5 - 20 times the intramuscular dose to yield equal effect.
  (3) Only small amounts are excreted in urine.
  (4) Evidence is indicated of ready degradation in liver, with major excretion via intestinal tract.

g) Miscellaneous:
  (1) Notable is the emetic action of hypotensive veratrum-alkaloids; the action is not central on the vomiting center of medulla oblongata; the effect remains after vagal section below nodose ganglion and is abolished by vagal section cephalad to nodose ganglion; action probably localized in nodose ganglion.
  (2) Irritant to mucous membranes; sternutatory (violent sneezing on contact).

h) Symptoms of poisoning: Burning of mouth, salivation, vomiting, diarrhea, headache, giddiness and weakness; death is by respiratory failure. Precautions: Use respirator. 1582

3) Phytotoxicity:
  a) The phytotoxic hazard is apparently very low. Transient and slightly toxic effect is reported in the case of certain cucurbits, for instance squash species and varieties. 482

4) Toxicity for insects: (Cevadine and veratridine are primarily responsible for insecticidal action.) 1859
  a) Quantitative:

Insect	Alkaloid	Route	Dose	Dosage	Remarks	
Oncopeltus fasciatus	Cevadine	Topical	LC_{50}	0.0005%		40
Oncopeltus fasciatus	Veratridine	Topical	LC_{50}	0.002%		40
Periplaneta americana	Germerine	Injection	LD_{50}	260 μg/g		2801
Periplaneta americana	Cevine	Injection	LD_{50}	88 μg/g		2801
Periplaneta americana	Germerine?	Injection	LD_{50}	11 μg/g	Crude fraction of Veratrum viride believed to contain germerine.	2801
Periplaneta americana	Jervine, Pseudojervine	Injection	Non-Toxic			2801

  b) Qualitative:
  10% and 20% dusts of sabadilla (ground seeds) are highly toxic to sucking plant bugs, e.g. Anasa tristis, Lygus spp., Blissus spp., harlequin bugs and leafhoppers of beans, potatoes, peas; effective vs. grapeleaf hopper, gypsy moth, Oncopeltus fasciatus, Melanoplus femur-rubrum, cattle lice, blunt-nosed leafhopper, black-headed fireworm, Pieris rapae and Trichoplusia ni. 1859 38,1125 378 1005

c) Toxicity of Veratrum viride alkaloids for insects: 1009

(1) LD_{50} (mg/g) of Veratrum viride extracts for Periplaneta americana; oral administration in baits:

Extract	Sample A	Sample B
Ether-soluble alkaloids	0.256	0.307
Total alkaloids	0.334	0.521
H_2O soluble alkaloids	--	0.335
Ether insoluble alkaloids	--	--
Arsenic trioxide (comparison)	1.445 mg/g	

(2) Mortality of Musca domestica (adult) sprayed with water soluble extracts of Veratrum viride:

% Ether-Soluble Extracts	% Mortality
0.023	87.0
0.018	77.0
0.011	74.0
0.0096	48.0
0.0056	43.0
0.0048	32.0
0.0028	28.0

(3) Mortality of Blattella germanica and Oncopeltus fasciatus with dusts of Veratrum viride:

Material	% Mortality Of	
	Blattella	Oncopeltus
Whole Veratrum powder (1.3% alkaloids)	52	--
Ether-insoluble alkaloids	0	0
Ether-soluble alkaloids 10%	100	100
Ether-soluble alkaloids 2%	52	--
Ether-soluble alkaloids 1%	15	86
Pyrethrum powder (0.9% pyrethrins)	100	--

(4) Aqueous extracts as contact sprays proved ineffective vs. Aphis rumicis and Myzus persicae.

d) Effectiveness of Sabadilla and Sabadilla-alkaloids vs. insects:

(1) Vs. Anasa tristis (laboratory tests): 3221

Material	% Mortality At Days After Treatment					
	1 day	2 days	3 days	4 days	6 days	8 days
Sabadilla (10% dust)	47.9	75.1	80.4	85.2	85.2	86.0
DDT (")	2.0	21.2	33.4	44.1	70.3	82.1
Control	0	0	0	6	6	10.1

(2) Vs. Oncopeltus fasciatus (10 day old adults) as dusts in pyrophyllite: 40

Toxicant	% Mortality 48 Hrs At Concentrations Of		
	1:100	1:500	1:1000
Veratrine	100	90	0
Cevadine	100	100	94.3
Veratridine	100	42.5	0
Cevine	7.5	0	2.5
Veratrine hydrochlorides	100	35.0	2.5
Oil fraction of seed	0	0	2.5
Control	2.5	0	2.5

(3) Cevadine, as dusts in pyrophyllite, vs. Oncopeltus fasciatus (10 day adults) and Melanoplus femur-rubrum; 40 insects per trial: 40

Dilution	% Mortality Of Oncopeltus	% Mortality 48 Hrs Of Melanoplus
1:100	100	--
1:500	100	--
1:1000	100	80
1:2000	100	55
1:3000	100	32.5
1:4000	97.5	25
1:5000	100	25
1:6000	100	--
1:7000	85	--
1:8000	50	--
Control	0	7

(4) Sabadilla alkaloids in kerosene vs. Oncopeltus fasciatus (10 day adults) 40 insects per trial: 40

Concentration	Veratrine		Veratridine		Cevadine		DDT	
	KD (1 hr)	Kill % 48 hr	KD (1 hr)	Kill % 48 hr	KD (1 hr)	Kill % 48 hr	KD (1 hr)	Kill % 48 hr
1:10	--	--	--	--	--	--	0	45*
1:33	--	--	--	--	--	--	0	5
1:100	--	--	--	--	--	--	0	0
1:250	--	--	36	95	--	--	--	--
1:500	--	--	14	35	--	--	--	--
1:1000	31	97	12	5	32	97	--	--
1:1500	12	27	--	--	28	78	--	--
1:2000	10	17	4	0	22	55	--	--
1:3000	--	--	--	--	14	37	--	--
1:4000	--	--	--	--	2	2	--	--
Control	0	0	0	0	0	0	--	--

*Mortality increasing at 72 hrs.

(5) Sabadilla and pyrethrum as dusts vs. Anasa tristis (adult) in field tests: 785

Sabadilla (%)	Diluent %	Alkaloids (%) (toxic)	% Kill 72 Hrs	Pyrethrum (%)	Diluent (%)	Pyrethrins (%)	% Kill 72 Hrs.
30	70	0.8	96	75	25	0.375	20.8
25	75	.67	90.2	62.5	37.5	.312	16.8
20	80	.54	73.3	50	50	.250	16.0
15	85	.4	60.0	37.5	62.5	.187	15.2
10	90	.27	45.6	25	75	.125	12.5
5	95	.13	20.4	12.5	87.5	.062	4.8
Control	--	--	1.1	--	--	--	.9

e) Synergistic action* of certain pyrethrum-synergists with sabadilla vs. Musca domestica; topical application: 271

Synergist	µg Synergist	µg Sabadilla	% Mortality 24 Hrs.
Piperonyl butoxide	5	0.5	50
"	10	1.0	77
Piperonyl cyclonene	5	0.5	32
"	10	1.0	56
Sulfoxide	5	0.5	48
"	10	1.0	72
MGK-264	5	0.5	14
"	10	1.0	53
IN-930	5	0.5	19
"	10	1.0	52
n-Propyl isome	5	0.5	38
"	10	1.0	52
Sabadilla control	--	0.5	8
"	--	1.0	19

* Toxicity of sabadilla was potentiated by the 6 tested pyrethrum synergists.

f) Pharmacological, pharmacodynamic, physiological, etc.; insects:

(1) Cevadine and veratridine are considered primarily responsible for action on insects. 40

(2) Primary action site is indicated as the neuraxon; on the giant axon of squid and on crab leg nerve (as on frog sciatic nerve) veratridine and cevadine prolong the negative afterpotential and delay repolarization, thus increasing, or potentiating, transmission at synapses by increased facilitation; response greater with cevadine; time constant greater with veratridine. 2805

(3) Cevadine and veratridine induce repetitive nerve impulse discharge after stimulus; in crayfish the effect may be induced by 0.1 - 1 ppm concentrations (higher concentrations induce spontaneous activity and bring about, at times, blockage of conduction). 2805

(4) Overall response is considered DDT-like, and has been attributed to increased escape of extracellular potassium ion, or upset of normal calcium balance in the neuraxon. 2805

(5) Cevadine and veratridine stimulated respiration slightly in Oncopeltus fasciatus. Disturbances of the respiratory enzyme systems are suggested; cytochrome oxidase and succinic dehydrogenase systems were stimulated by sabadilla alkaloids as measured by sensitivity of breis of poisoned insect tissues to cytochrome C, in terms of succinic dehydrogenase activity. 568 1441

g) Action on beneficial insects:

(1) Reported as safe and without hazard for Apis mellifera in a few minutes after application to plants. 3099
However, sabadilla is highly toxic to bees. 927

h) Reports of field experiences in control of economic insects:

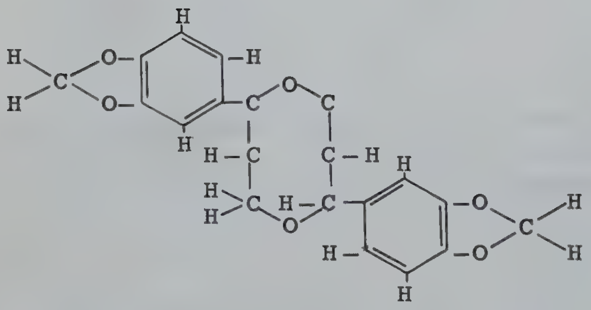
(1) Vs. Nezara viridula: Ineffective. 1099

(2) Vs. Anasa tristis: Highly effective; superior to pyrethrins. 3053

(3) Vs. Lygus oblineatus } Some control on seed alfalfa. 2211
(4) Vs. Adelphocoris sp. }
(5) Vs. Empoasca fabae: Highly effective. 38
(6) Vs. Pieris rapae, Trichoplusia ni: 10% dusts yielded 84.5% control (DDT gave 88.2%, DDD gave 87%, rotenone gave 85.8%, lindane gave 84.2%, Ryania gave 83.1%, toxaphene gave 80.8%, pyrethrum gave 78.6%, lead arsenate gave 77.6%, chlordane gave 72.6%, methoxychlor gave 60.9%). 796
(7) Vs. climbing cutworms: Ineffective (on peaches). 471
(8) Vs. Hylemyia brassicae, H. floralis: Ineffective. 796
(9) Vs. Epilachna varivestis: No better than DDT which is relatively ineffective. 870

160

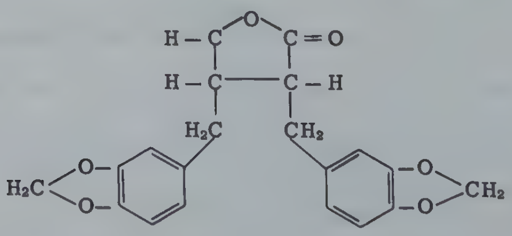
SESAMIN (Asarinin); also Sesame oil, Sesamolin.



Molecular weight 352.334

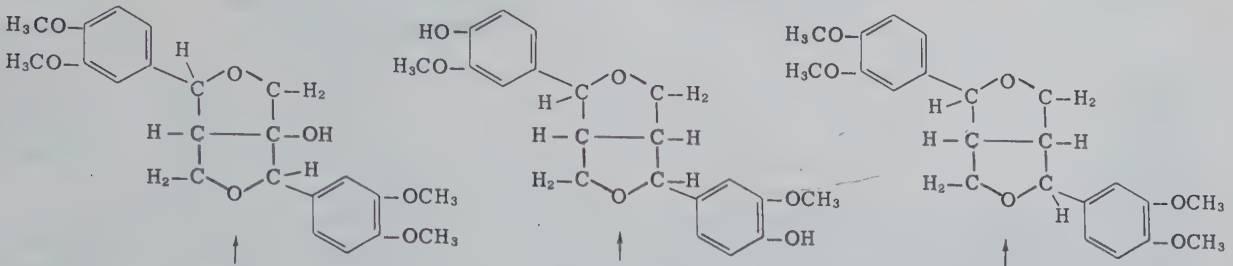
GENERAL [Refs.: 891, 3037, 1346, 1347, 2454, 1151, 353, 2231, 2120, 461, 563, 1348, 1778, 232, 376, 1779, 1344, 2137, 2136, 1801]

Sesame oil has been recognized for some time to be a highly effective synergist, potentiating the lethal action of pyrethrins without affecting the pyrethrin "knockdown" action. Sesamin, a crystalline fraction of sesame oil, is the active synergistic principle of sesame oil in which it is present to ca. 0.25%. The oil (and thus sesamin) is derived from the seeds of Sesamum indicum, widely used as a food and seasoning both in the form of the seed and as the oil. A laevo-rotatory optical isomer of sesamin, namely asarinin, occurs in the bark of the southern prickly ash and in other plants, and like sesamin possesses active synergistic properties with pyrethrins. Neither sesame oil, sesamin or asarinin is itself insecticidal. All are synergists for pyrethrins which they spare, and whose insecticidal action they augment. Sesamolin, another component of sesame oil, identical in structure to sesamin save that one of the methylenedioxyphenyl-groups is attached to the central nucleus by an ether linkage, is even more potent a synergist for pyrethrins than sesamin itself vs. Musca domestica. The synergistic properties of sesamin and related substances are associated with the methylenedioxy-groups, since related compounds which do not possess this group are inactive as synergists. Hinokinin, for example, from Chamaecyparis obtusa (an oriental conifer) is virtually of the same synergistic potency aslaevo-asarinin:



Other related substances, for example gmelinol, eudesamin and pinoresinol are inactive as synergists.

Thus, from sesame oil three substances have been isolated: Sesamin, sesamolin and a sterol, sesamol, of which the first two are highly active synergists. However, it is unnecessary to isolate the active principles for synergistic action. Sesame oil, as such, may be used. Sesame oil is a glyceride oil. Sesamin does not synergize with isobornyl thiocyanoacetate vs. Musca domestica.



Gmelinol

Pinoresinol

Eudesamin

PHYSICAL, CHEMICAL [Refs.: 232, 376, 1347, 1348, 1671, 385, 469, 224]

Sesamin is a crystalline solid; m.p. 122.5°C (122.7°C); dextro-rotatory $[\alpha]_D^{22°C} = +68.32$; insoluble in water; soluble in most organic solvents; slightly soluble in petroleum ether; converted to the optical isomer, isosesamin, by action of hydrochloric acid.

1) Formulations: In aerosols as sesame oil 6%, pyrethrin extract (20% pyrethrins) 4% in dichlorodifluoromethane; DDT may or may not be added.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Sesame oil is edible and non-toxic.

2) Toxicity and synergistic action of sesame oil and its components and related compounds for insects:
   a) Effectiveness of sesame oil and fractions, with and without pyrethrins, in refined kerosene oil vs. Musca domestica (150 adult insects per test); concentrate of pyrethrins 1 mg, sesame oil (and fractions) 10 mg per cc: 891 1346

Substance	% "Knockdown" 10 Minutes	% Mortality 48 Hrs.
Sesame Oil	0	2
Pyrethrins	99	21
Pyrethrins + Sesame Oil	100	57
" + Fraction I	100	100
" + Fraction II	100	91
" + Fraction III	100	21
" + Fraction IV	100	29

Concentrate of pyrethrins 1 mg, sesame oil fractions 2.5 mg per cc in refined kerosene + 10% of acetone 150 adult Musca per test.

Pyrethrin	100	20
Sesamin (crystalline fraction)	0	5
Pyrethrins + sesamin (crystalline fraction)	100	85
" + " (non-crystalline ")	100	89

   b) Effect of sesamin and related substances on the insecticidal action of pyrethrins vs. Musca domestica: 1346

Material	Concentrations (%) Of		Ratio	Average Mortality After 24 Hrs (%)
	Synergist	Pyrethrins		
Sesamin	0.2	0	-	4
Sesamin + pyrethrins	0.2	0.05	4	84
Isosesamin	0.2	0	-	5
Isosesamin + pyrethrins	0.2	0.05	4	87
Asarinin	0.2	0	-	14
Asarinin + pyrethrins	0.2	0.05	4	88
Pyrethrin control	0	0.05	-	25
Pinoresinol	0.18	0	-	1
Pinoresinol + pyrethrins	0.18	0.05	3.6	12
Dimethyl pinoresinol	0.2	0	-	1
Dimethyl pinoresinol + pyrethrins	0.2	0.05	4	17
19% Diacetyl pinoresinol	0.03	0	-	2
19% Diacetyl pinoresinol + pyrethrins	0.03	0.05	0.6	11
Pyrethrin Control	0	0.05	-	25

c) Synergistic effect of sesamin and related substances vs. Musca domestica after Ref. 2231.

Compound	Ratio to Pyrethrins	Difference Between % Kill Of Mixture And Pyrethrins Alone At Same Concentration
Sesamin	4	+ 59
Isosesamin	4	+ 62
Asarinin	4	+ 63
Gmelinol	2	+ 2
Isogmelinol	2	+ 1.5
Pinoresinol	3.6	- 7
Pinoresinol dimethyl ether	4	- 2
Diacetyl pinoresinol	0.6	- 8
Eudesamin	2	+ 14
Sesamolin	0.2	+ 84
3,4-Methylene dioxyphenol	5	+ 3

d) Sesamin, sesamolin and sesamol* with pyrethrins and allethrin as kerosene sprays vs. Musca domestica (adult); at concentrations used sesamin and sesamolin were non-toxic: 1151

Material	LC_{50} (mg/deciliter) Insecticide	Insecticide + Adjunct	Rel. S.E. Of LD_{50} (%)	Toxicity Ratio	Log Of Ratio	Minimum (log) Required To Show Synergism
Pyrethrins	438 ± 50	-	11.3	1	0	-
" + sesamin	54.5 ± 8.6	54.5	15.9	8.04 ± 1.57	0.905	0.166
" + sesamolin	14.1 ± 3.2	14.1	22.6	31.0 ± 7.8	1.492	0.215
" + "	42.1 ± 7.5	8.4	18.0	10.4 ± 2.2	1.018	0.181
Allethrin	69.5 ± 6	-	8.6	1	0	-
" + sesamin	46.0 ± 5	46.0	10.8	1.51 ± 0.21	0.179	0.117
" + sesamolin	48.9 ± 4.9	48.9	10.1	1.42 ± 0.19	0.153	0.113
" + "	53.3 ± 5.4	10.7	10.2	1.3 ± 0.17	0.115	0.114

*Sesamol does not synergize with pyrethrins.

3) Pharmacological, pharmacodynamic, physiological, etc.; insects:

a) The general principle of synergistic action may be expressed as follows: Combinations of compounds which have higher biological activity than the sum of the activities of the individual components are said to be synergistic. 3008

b) Sesame oil, sesamin and sesamolin are excellent examples of synergistic substances with pyrethrins, since per se they are non-toxic for insects yet potentiate greatly the lethal effects of pyrethrins.

c) The mechanism of synergistic action remains largely unknown. For sesamin, the synergistic effect remains when all physical effects of droplet size, stabilization, etc. are eliminated. 2432

d) The toxicity of pyrethrins is increased by a factor of at least 3 times when sesamin is added to pyrethrins in up to equimolecular proportions; further increase of sesamin does not increase the effect. (The foregoing is true in the case of Aëdes aegypti in flight through insecticide + synergist mists.) Suggested is a surface complex between synergist and insecticide at the peripheral nerve sheath interfaces which reorientates the pyrethrin molecule to bring about more effective discharge of nerve resting potential at the interface. 2432

e) The sharp limitation of synergistic action noted for sesamin at equimolecular proportion with pyrethrins vs. flying Aëdes aegypti has been confirmed vs. Sitophilus granarius crawling on deposits made by oil base sprays. The limiting relative potency is attained at equimolecular proportions not only for sesamin but for N-isobutyl undecyleneamide, ethylene glycol ether of pinene, piperonyl cyclonene, n-propyl isome and N-(2-ethylhexyl)-bicycle [2,2,1] -5 heptene-2,3-dicarboximide but not for piperonyl butoxide. 249

161

SODIUM ARSENATE (Sodium meta-arsenate)

$Na_2HAsO_4 \cdot 7H_2O$; $NaAsO_3$

GENERAL

(Also consult the section in this work titled Arsenic, Arsenicals.)
[Refs.: 353, 2815, 1059, 757, 129, 3350]

A compound which has been used as an insecticide, herbicide and rodenticide. As the foregoing statement suggests, sodium arsenate is toxic to most forms of animal and plant life. Solutions of sodium arsenate have been employed to kill termites in their galleries. A substance which must be handled with precaution and which requires the label "Poison", sodium arsenate must meet the following standard: A content of at least 50% arsenic (expressed as the element) which is equivalent to 65% arsenic trioxide. Although highly poisonous the compound is less so than sodium arsenite.

PHYSICAL, CHEMICAL

A colorless and odorless salt; readily soluble in water; specific gravity = 2.301; the arsenic is in pentavalent form; ordinarily obtainable as a dry powder.

TOXICOLOGICAL

1) Acute toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Frog	or	LD	600		1035
Frog	sc	LD	200		1035
Rat	ip	MLD	34.7-44.6		1056
Minnows	Medium	ca. MLC	250 ppm	As arsenic element.	1276

a) The toxic threshold concentration for Polycelis nigra, a fresh water platyhelminth (planarian) is 670 ppm as $AsO_4^{\equiv}$; the threshold concentration for immobilization of Daphnia magna, a crustacean of fresh waters, is 18 - 31 ppm in lake water at 25°C. 1727, 68, 2400

2) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:
   a) Consult the general treatment Arsenic, Arsenicals.

3) Phytotoxicity:
   a) Phytotoxic hazard extremely great; used as an herbicide.
      (1) The solubility of the compound in water makes it too hazardous to use directly on plants.
      (2) Like other arsenicals, tends to accumulate in soil.

4) Toxicity for insects: 2219,2220

Insect	Route	Amount (μg/g) To Yield Mortality (%) Indicated 0%	50%	100%	LD_{50} ca. (mg/k)
Anasa tristis	Injection	10	20	40	
Ceratomia catalpae (larva)	Injection	10	20	30	
Periplaneta americana	Topical	♂30; ♀150	♂ 100; ♀500	♂300; ♀1300	♂100 ♀>1600
Periplaneta americana	Oral	♂80; ♀600	♂ 250; ♀2000	♂600; ♀6000	♂<50 ♀500
Periplaneta americana	Injection	♂23; ♀35	♂ 30; ♀50	♂ 45; ♀70	♂25 ♀42
Popillia japonica	Topical	400	850	1700	
Popillia japonica	Injection	20	50	100	

a) Toxicity for beneficial insects:
   (1) Exceedingly hazardous (as are all arsenicals) for Apis mellifera; oral LD_{50} as arsenic element = 1.8 μg/bee. 1852

b) Pharmacological, pharmacodynamic, physiological, etc.; insects:
   (1) Consult the general treatment, "Arsenic, Arsenicals."

162

SODIUM ARSENITE ("Sodium meta-arsenite.")

(Formerly thought of as being sodium meta-arsenite, Na_2HAsO_3; now considered to be (probably) a solid solution of Na_3AsO_3 (Molecular weight 192) and $NaAsO_2$ (Molecular weight 129.9.)

GENERAL [Refs.: 353, 129, 2815, 1059, 757, 2120, 484, 3214, 2444, 2447, 3190]

An insecticide which has long been used as an ingredient in poison baits for grasshoppers, locusts, mormon crickets, roaches, ants, etc., and in stock dips. Because of intense phytotoxic hazard it is not employed on crops or plants. Indeed, sodium arsenite has been used as a general, non-selective herbicide and weed-killer. A potent, hazardous, dangerous poison for man, animals, and plants. Has been employed as a rodenticide. Extremely hazardous to domestic animals and wild-life. It is recommended that all animals be kept from treated areas for at least three months in dry weather, or until at least 4 heavy rains have fallen. For use vs. the mormon cricket, baits containing sodium fluosilicate have largely superseded sodium arsenite. Largely superseded by chlorinated hydrocarbons in control of Melanoplus mexicanus, M. bivittatus, Camnula pellucida, Melanoplus differentialis, Nemobius fasciatus, Dociostaurus sp., against which it was once widely employed.

PHYSICAL, CHEMICAL [Refs.: 484, 353, 129, 2120]

A white to gray hygroscopic powder which is decomposed by moisture and atmospheric carbon dioxide; specific gravity 1.87; readily soluble in water; slightly soluble in alcohol; formed by dissolving arsenic trioxide in sodium hydroxide solution. Depending on the ratios of reactants, products range from the monosodium compound $NaAsO_2$ to the trisodium compound Na_3AsO_3; a standard formula for making so-called liquid sodium arsenite calls for 4 pounds of white arsenic and 1 pound of sodium hydroxide per gallon of solution. Contains 82% As_2O_3.

1) Formulations: To a maximum of 3% in sugar or honey as a bait for ants; in solution as a weed-killer; as a solid, per se.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) An exceedingly potent arsenical poison. Application of a 0.6% solution at 110 - 120 gallons per acre has proved dangerous to livestock grazing on treated areas until after heavy rains have fallen. 2982
   b) Generally to be considered more toxic than arsenates, since it is believed that for arsenical poisoning to occur, arsenates must first be reduced to arsenites, and arsenic-pentavalent changed to arsenic-trivalent. 3107, 1221
   c) The lethal dose for mammals (oral intake) has been quoted as 10 - 50 mg/k. 129,2447
   d) Reported to have been used at 2 - 3 ppm in water to control aquatic weeds without hazard to man or animals. 2997
   e) Quantitative

Animal	Route	Dose	Dosage	Remarks	
Mouse ♂	sc	LD_{50}	12.3 ± 7.0		209
Mouse ♂	sc	LD_{50}	11.2 ± 4.3		209
Mouse ♂	sc	LD_{50}	9.8 ± 0.59		209
Mouse ♂	sc	LD_{50}	12.0 ± 0.55		209
Mouse ♂	sc	LD_{50}	10.5 ± 0.37		209
Mouse ♂	sc	LD_{50}	9.8 ± 0.55		209
Mouse ♀	sc	LD_{50}	12.5 ± 5.0		209
Mouse ♂	iv	LD_{50}	10.7 ± 0.42		209
Rat	ip	MLD	9.6 - 10.7		1056
Fish	Medium	Toxic	1 - 2 ppm	Used in control of aquatic weeds.	2200
Fish	Medium	No Effect	2.5 - 5.0 ppm		168
Fish	Medium	No Effect	10 ppm	Used to control aquatic weeds.	2065
Minnows	Medium	LC	20 ppm	As elemental arsenic.	1276
Fish	Medium	Non-Toxic	4 ppm		353

(1) More toxic than sodium arsenate (solutions containing equal quantities of arsenic element) for the fishes Phoxinus phoxinus and Salmo gairdneri shasta. In solutions of sodium arsenite (20 ppm As) minnows survived a mean period of 36 hrs. before "overturn"; in sodium arsenate minnows survived 250 ppm As for 16 hrs. before "overturn" (see below). 1276

1) Acute toxicity for higher animals (Continued)

Concentration (ppm As)	Temperature °C Minimum	Temperature °C Maximum	pH	Mean Immersion Before Overturn (Minutes)	Mean Toxicity (100 Times Reciprocal Of Immersion Time)
			Sodium arsenite		
953	11.5	17.5	8	54.6	1.83
669	13.0	13	7.9	80	1.25
478	12.2	17	8	96.1	1.04
384	11.5	13	8	114.2	.88
290	11.5	17	8	186	.54
195	12.2	17	8.1	248	.40
98	11.5	13	8	483	.21
47.5	14.3	18.2	7.8	1142	.088
17.8	12.3	-	7.8	2174	.046
			Sodium arsenate		
2970	16.8	19.4	8.3	205	.488
2370	17	22.5	8.3	248	.402
1780	16.5	20	8.3	294	.340
1210	15.5	19	8.2	442	.226
820	13	-	7.9	467	.214
610	17.3	21.3	8.0	543	.184
234	16.1	20	8.2	951	.105

Na arsenite in concentration = to 1 ppm As kills Daphnia magna (crustacea)
Na arsenate threshold concentration to immobilize Daphnia = 31 ppm (14 ppm As)

(2) Has proved toxic to dogs in drinking water at a concentration = to 5 ppm As; rats and pigs survived this concentration used as counteractant in selenium poisoning. 537

f) Chronic toxicity:
(1) Consult general treatment titled Arsenic, Arsenicals.

g) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:
(1) Consult general treatment titled "Arsenic, Arsenicals."
(2) Arsenite is reported to inhibit pyruvate oxidase enzyme systems in vertebrate tissues; arsenate, on the contrary, is reported not to inhibit enzymes. 2489 164

h) Hazard for wildlife:
(1) Highly toxic to animals. When used in locust control in Africa it has been the cause of high kills of wild game. Birds have been known to die from eating sodium arsenite-poisoned insects. 353
(2) All animals should be kept for 3 months (in dry weather) from areas where sodium arsenite has been used as an herbicide.
(3) At 1.9 - 3.0 ppm (arsenic trioxide equivalent) has killed fish-food-organisms. To 1.9 - 3.9 ppm as As has proved fatal to chironomid larvae, mayfly nymphs and fresh water shrimps on which fish feed. 2716 3021,1276

i) Phytotoxicity:
(1) The phytotoxic hazard is very high. Plants, however, are killed only by direct contact with sodium arsenite and not by any systemic action. 353 129
(2) 2 gallons of commercial sodium arsenite (8 lbs arsenious oxide per gallon) diluted 1:40 with water and applied at the roots kills a barberry bush, with all parts of the dead plant showing arsenic at from 0.007% to 0.188%. The same concentration is fatal to many kinds of plants. Arsenic content of soil so treated declines from 0.676% (at treatment) to 0.04% after 14 months with a 30-inch rainfall. 2785

2) Toxicity for insects:
a) Active both as a stomach and as a contact poison. 2079,1254,3370,2407,2408
b) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Euxoa segetum (5th instar)	or	MLD	30 - 135 µg/g		2847
Euxoa segetum (larva)	or	MLD	140 µg/g	As arsenic element.	3208
Locusta migratoria migratorioides	or	MLD	30 - 135 µg/g		2847
Locusta migratoria migratorioides	or	MLD	30 µg/g	As arsenic element.	3208
Pieris brassicae (5th instar)	or	MLD	30 - 135 µg/g		2847
Pieris brassicae (larva)	or	MLD	40 µg/g	As As element.	3208
Pieris rapae	or	MLD	ca. 25 µg/g	As arsenic element.	3317
Periplaneta americana	inj	LD	100µg/1.2 gram insects	As As_2O_3.	2440
Musca domestica	or	LD_{50}	180 µg/g	As As_2O_3; 140 µg/g as arsenic element.	2463

c) Toxicity of trisodium arsenite for Musca domestica, oral administration; adult insects 1 day after pupal emergence: 2463

Zone	Body Weight (mg)		Survival Time (Hrs.)		Dosage In mg As_2O_3/g	
	Mean	Range	Mean	Range	Mean	Range
Lethal	13.5	13.3-13.6	6	5 - 8	0.273	0.258-0.293
Intermediate	15.1	13.1-18.0	6	1 - 15	.216	.139- .243
	14.6	13.1-17.9	20	16 - 50	.205	.128- .233
	15.8	13.6-18.6	92	44 - 51	.187	.108- .233
	15.5	12.5-19.8	Survived		.159	.110- .250
Sub-lethal	16.9	14.3-19.2	Survived		0.09	.060- .103

d) Mortality of caged crickets, Gryllus assimilis, supplied with bran bait containing 100 g. bran, 95 - 105 cc water, sodium arsenite and molasses in varying amounts: 2325

Amount (g) Sodium arsenite	Amount Molasses (cc)	% Mortality After		
		24 Hrs	48 Hrs	72 Hrs
12	16	32	43	64
6	32	14	28	40
5	16	16	26	40
5	16 + orange	12	23	31
4	0 (but amyl acetate 1 drop)	10	20	30
White arsenic				
12	16 + orange	22	38	63
5	16 + orange	8	13	32
Sodium fluoride				
5	16 + orange	30	66	84
Sodium fluosilicate				
12	16	59	86	92
12	16 + orange	61	81	88
5	16 + orange	46	75	89
2½	16	28	44	52

e) Sodium arsenite and other compounds, comparative toxicity for Melanoplus via the oral route in suitable baits: 2611

Toxicant	LD_{50} (μg/g) For		
	Melanoplus bivittatus	M. femur-rubrum	M. differentialis
Sodium arsenite	15*	100	--
Arsenic trioxide	26**	360	90
Sodium fluosilicate	100**	120	--
Sodium fluoride	40	--	110

*At 0.4 mg/g survival time = 20 hrs.
**At 0.4 mg/g survival time = 33 hrs.

f) Pharmacological, pharmacodynamic, physiological, etc.; insects:

(1) Contact effectiveness: Antennae are the fastest portal of entry for, in case of Locusta; intersegmental membranes most rapid entry way for dusts of sodium arsenite in Schistocerca. 1973

(2) Anabrus after contact and prevented from grooming and eating applied dust, may be dead in paralysis within 12 hrs. Contact toxicity is enhanced by humidity. 1227

(3) Schistocerca died in 10 - 11 days from application to highly sclerotized surfaces. 2407,2408

(4) Penetrated Periplaneta cuticle 4 times as fast as As_2O_3.

(5) Via the oral route in Periplaneta: Absorbed into hemolymph and tissues via the proventriculus; major absorption in midgut, little in hind-, and less in foregut. 970 1592

(6) Euxoa, Euproctis larvae avoid foliage treated with sodium arsenite; Locusta migratoria avoids food treated with sodium arsenite. 1592

  (a) Euxoa segetum, after ingesting sodium arsenite, vomited most of the toxic meal within an hour. Similar response from Bombyx mori; Pieris brassicae readily accepted and did not vomit sodium arsenite poisoned food. 814,3208 586

  (b) Acted as purgative for Euxoa and Pieris but not for Locusta. 3208

  (c) Absorption varies with species; this may account for widely divergent LD values.

  (d) Highest toxic effect exerted in species with acid gut pH, for instance Locusta migratoria with stomach pH = 6.8. 814

  (e) Euxoa segetum resisted sodium arsenite because of regurgitation, purgation, low rate of intestinal absorption and excretion via malpighian tubules. Added to these was the avoidance of sodium arsenite treated food in case of Euxoa (as well as by Euproctis) which kept the intake of toxicant low. 814

(7) Much more toxic than sodium arsenate for Malacosoma and Datana larvae. 60% more effective than sodium arsenate or arsenic oxide as a depressant of respiration in Leptinotarsa decemlineata. 454

(8) Symptoms of intoxication (sequence):

  (a) Periplaneta americana: I) Decrease in activity; II) loss of equilibrium; III) loss of posture recovery reflexes; IV) general asthenia; V) weak response to stimulus; VI) failure of response to stimulus; VII) death.

- (9) Histopathology:
  - (a) Destruction of midgut epithelium (Vanessa urticae, Prodenia eridania, Locusta) an effect not ob- 2510
    tained in Pieris brassicae or Porthetria dispar. 1973,1592
  - (b) Marked changes in cells of haemolymph; susceptibility enhanced by haemolymph cell blockage with 3383
    carbon-black. 2762
  - (c) Via ingestion, depressed heart rate of Bombyx mori; via injection, accelerated the rate. 456
- (10) Biochemical:
  - (a) Marked affinity of arsenite ions for sulfhydryl groups of proteins, enzymes is reported. 999,586,3191
  - (b) Depressed by 30% to 50% O_2 consumption of isolated Carpocapsa pomonella tissues (fat body, 1243
    muscle).
  - (c) Depresses dehydrogenase activity of tissues in various insects. This effect is attributed by some 2847
    to tissue destruction and protein denaturation. 2762,2440,3107

g) Miscellaneous

- (1) Formerly employed in 1% baits to control Cirphis unipuncta, Laphygma frugiperda and Prodenia 2226
  eridania larvae.
- (2) In cattle dips 0.64% is the minimum effective concentration to control Boöphilus decoloratus (some 353
  strains show resistance).
- (3) Very effective vs. termites. 353

163

SODIUM FLUORIDE

Na F Molecular weight 42.0

GENERAL [Refs.: 353, 2815, 1204, 757, 2120, 129, 484, 1828, 1801]

A highly toxic and hazardous inorganic toxicant which has been long employed as a cockroach poison and which has a very effective action against various lice of poultry. Sodium fluoride is an insecticide of highly specialized application. Great phytotoxicity limits its employment largely to poison baits or dusts in control of household and other insects. Because of the hazard of mistaking sodium fluoride for such food products as sugar, baking powders, salt, etc., the commercial product in the United States must by law be colored blue to prevent confusion with comestibles of similar appearance.

PHYSICAL, CHEMICAL

A colorless, crystalline solid, or a pure-white powder; odorless; m.p. 980°C; b.p. 1700°C; specific gravity 2.8; v.p. extremely low; soluble in water to 1 part in 25 parts, 4.22 g in 100 g at 18°C or 4% w/w at 15°C; slightly soluble in alcohol; corrodes glass in aqueous, acidic solution.

1) Formulations: (Not generally used in combination with other insecticides) as the commercial salt 93% - 99% pure; insect dusting powders; poison baits; 3% solutions; wet "crayons". Usually blended with borax, pyrethrum and inert diluents. Particle size 5 - 10 micra.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) Highly toxic to vertebrate forms; lethal dose for man = 75 - 150 mg/k; severe symptoms recorded in man 2120
   following dosages of 250 - 450 mg, and death after dosages of 4 g. The symptoms attending intake of 230 - 2221
   450 mg are severe for 36 hours or more if the substance is retained. The lowest recorded fatal dose is 851
   reported as 2 grams. A 2% solution kills the superficial cells of mucous membranes. Local actions, upon 3166
   ingestion, include a marked gastro-enteritis. Dusts of sodium fluoride are distinctly hazardous wherever handled in such a way that the substance is made air-borne. Suggested maximum concentration dust = $0.2\ mg/m^3$. Insecticides and rodenticides containing sodium fluoride are almost solely responsible for fluoride poisoning in human beings and domestic animals. 1 ppm = probable threshold value below which, in drinking water, no harm results to animals.

b) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Frog	sc	MLD	400		2842
Mouse	or	LD	80		2784
Mouse	sc	LD	70		2784
Mouse	sc	LD	125	Death in 32 minutes.	1038
Rat	or	LD_{50}	ca. 200		1951
Rat	sc	MLD	125		2312
Rat	ip	MLD	28-35		2695
Guinea Pig	or	MLD	250		2842
Guinea Pig	sc	MLD	400		2842
Rabbit	or	MLD	100-200		2695
Rabbit	or	MLD	200		2312
Rabbit	or	LD	500		1676
Rabbit	iv	MLD	87.5		1941
Rabbit	iv	LD_0	75		1941
Rabbit	iv	LD_{80}	87.5		1941
Rabbit	iv	LD_{100}	90		1941
Cat	sc	LD	13.7	Death in 2 hours.	1038
Dog	or	MLD	50-100		2695
Dog	sc	MLD	150-160		1038
Dog	im	MLD	31-50		2695
Dog	iv	MLD	80		2695
Minnows	Medium	No Effect	17.1 ppm	Exposure of 1 hour.	2400
Goldfish	Medium	Survived	100 ppm	More than 4 days exposure.	2400
Goldfish	Medium	Survived *	1000 ppm;	*Survived (in hard water) 60-102 hrs before succumbing.	2400
Man	or	LD	75-150		2221
Man	or	(?) LD	5g/subject		353

c) Some reported effects of fluoride in drinking water; various animals: 2954

Concentration Of Fluoride (ppm)	Dose	Animal	Effect
1.0	--	Cattle	No effect.
1.0	--	Sheep	Toxic.
--	0.4 mg/k	Cattle	No effect.
--	1.0 mg/k	Rat	Mottling of teeth.
--	1.0 mg/k	Cattle	Mottling of teeth.
--	3.0 mg/k	Cattle	Bone damage; death.
4.0	--	Sheep	Mottling, pitting of teeth.
6-16	--	Pigs, etc.	Severe mottling of teeth.
11.8	--	Cattle	Mottling of teeth.
18	--	Cattle	Progressive fluorosis.
44-61	--	Sheep	Chronic fluorosis.
50	--	Hamster	Dental fluorosis in 10 weeks.
55	--	Cattle	Aversion to drinking water.
--	60 mg/day	Sheep	Tooth, bone effects.
--	120 mg/day	Sheep	Threshold for intoxication.
--	200 mg/day	Rabbit	Death.

d) At fluoride ion concentrations of 1.7 - 1.8 ppm, 50% of human subjects (children) showed mottled teeth. Mottling to some extent has been reported at F^- concentrations ranging from 0.2 - 2.0 ppm. At 4.4 - 12 ppm chronic fluorosis and skeletal effects are reported. At 115 ppm considered sub-lethal; at 180 ppm toxic to man in drinking water; at 2000 ppm lethal to man in drinking water. 2954

2) Chronic toxicity, higher animals:

a) Rats: Toxicity first apparent at level of 500 ppm in the diet; some deaths at 500 ppm; at 900 ppm 100% mortality in 10 days. At 25 ppm striations appear on tooth enamel. As fluorine, 0.0904%/day in the diet or water brings death in 9 - 11 days. 728 2888

b) Chronic toxicity is confined to teeth, bones. 851,545

(1) Enamel defect (mottling) on excessive intake occurs during tooth development period, from birth to ca. 12th year in man.

(2) To 1.8 ppm fluoride: Minor changes in teeth apparent to skilled observers; at amounts greater than 1.8 ppm tooth mottling is easily recognized; with high fluoride content a brown stain may develop. At concentrations productive of marked mottling, pitting may also occur.

(3) Tooth effects constitute one of first signs of chronic fluorosis.

(4) At higher and more prolonged intake, bones become opaque to Roentgen-rays without known disability or pathology.

(5) Pronounced chronicity effects: Bone structure deformation with thickening, roughening and excessive

growth especially at muscular attachment points. Limitation of movement (chiefly of spine) may ensue. Symptoms: Anorexia, bone fragility, stiffness of hands, cachexia, and respiratory paralysis attend chronic fluorosis.

3) Symptoms of intoxication: Salivation, stomach pain, nausea, vomiting, diarrhoea; the foregoing are followed by muscular weakness, epileptiform convulsions (clonic), collapse; death from respiratory failure, cardiovascular collapse, myocardial failure. 851 1221
   a) Rigor mortis is quick after fluoride-induced acute toxicity. 851,1221
   b) Treatment of acute poisoning includes gastric lavage, giving by mouth of calcium salts, for example dilute $CaCl_2$ or calcium gluconate intramuscularly; milk is also useful. 1221 2806

4) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:
   a) For detailed treatment consult Fluorine, Fluorides, Fluosilicates, Fluoaluminates, in this work.

5) Phytotoxicity:
   a) Highly phytotoxic; too toxic for safe use on plants because of high solubility in water. Used as a non-selective herbicide. Sodium fluoride, tested at 1, 25, 50, 100, 200, 400 ppm (as fluoride) in sand cultures of lemon cuttings induced at 400 ppm, severe leaf injury and defoliation; at same concentration for orange cuttings, induced chlorophyll loss and reduction in leaf size. 353,2120 129 82

6) Toxicity for insects:
   a) Sodium fluoride is a potent stomach poison with some contact toxicity for insects in which it acts as a nerve toxicant and direct destroyer of stomach and gut epithelium. Used in control of roaches, ants, silverfish, poultry lice, dog fleas and wood-boring insects. Also used in some pastes and mucilages.
   b) Quantitative
      (1) For Periplaneta americana, average weight ♂ 0.9(0.7-1.15)g, ♀ 1.3(1.0-1.9)g: 2219

Route	Amount (µg/g) To Yield Mortality Indicated		
	0%	50%	100%
Contact	♂160; ♀200	♂250; ♀500	♂ 350; ♀850
Oral	♂100; ♀200	♂300; ♀1000	♂1300; ♀3500
Injection	♂ 80; ♀100	♂120; ♀140	♂ 150; ♀170

Insect	Route	Dose	Dosage	Remarks	
Apis mellifera (adult)	or	LD$_{50}$	6.0 µg/bee	As fluoride.	290
Blattella germanica	Topical (dust)	LDeposit$_{50}$	130 µg/cm^2	Dust directly applied to insect.	2357
Blattella germanica	Dust, Environment	LDeposit$_{50}$	40 µg/cm^2	Cage environment dusted.	2357
Bombyx mori (4th instar)	or	LD$_{50}$	110-150 µg/g		2819
Melanoplus bivittatus	or	LD$_{50}$	ca. 40 µg/g	Fed in bait.	2611
Melanoplus differentialis	or	LD$_{50}$	110 µg/g	Fed in bait.	2617,2611
Periplaneta americana	or	MLD	156-780µg/insect		3029
Periplaneta americana	Topical (dust)	LD$_{70}$ 10 days	1833µg/insect; 1763µg/g	Insects entering treated area at will.	2181
Blattella germanica	Topical (dust)	LD$_{70}$ 4 days	158µg/insect; 1375µg/g	Insects entering treated area at will.	2181
Periplaneta americana ♂	Contact	LD$_{50}$	>2000 µg/g		2220
Periplaneta americana ♀	Contact	LD$_{50}$	1200 µg/g		2220
Periplaneta americana ♂	or	LD$_{50}$	300-400µg/g	By injection into stomach.	2220
Periplaneta americana ♀	or	LD$_{50}$	100-200µg/g	By injection into stomach.	2220
Periplaneta americana ♂	inj	LD$_{50}$	140 µg/g	By injection into blood.	2220
Periplaneta americana ♀	inj	LD$_{50}$	250µg/g	By injection into blood.	2220
Daphnia magna (crustacea)	Medium	Toxic Threshold	504 ppm		2400

(2) Vs. Blattella germanica; dusted, or insects shaken in a jar with sodium fluoride dust: 777

Stage	Deposit (mg/cm^2) (Dusted)	% Mortality After		Average Survival Time (Hrs)		
		24 Hrs	96 Hrs	♂	♀	♂♀
1st Instar	0.81	100	100	-	-	0.6
2nd Instar	0.81	100	100	-	-	1.3
4th, 5th Instar	0.81	100	100	-	-	2.0
6th, 7th Instar	0.81	5	64	26.5	71.7	-
6th, 7th Instar	1.63	81	100	10.7	16.4	-
Adult	1.63	100	100	2.3	2.9	-
Adult	0.81	78	100	4.9	19.1	-
Adult	0.47	62	100	7.6	23.0	-
Adult	0.19	46	100	7.7	28.8	-
Adult	(Shaken in jar with dust)	100	100	0.37	0.69	-

(3) Sodium fluoride with other substances vs. Blattella germanica: 777

Material and Proportions	% Mortality After 24 Hrs	96 Hrs	Average Survival Time (Hrs) ♂	♀
Pyrethrum extract 1.4%, NaF 4%, Lube oil 6%, pyrophyllite	100	100	2.7	7.7
Pyrethrum 12.5%, NaF 25%, pyrophyllite 62.5%	100	100	3.6	4.5
" 12.5%, " 25%, bauxite 62.5%	100	100	3.1	8.8
" 10%, " 20%, pyrophyllite 35%, bauxite 35%	90	100	3.4	14.8
" 10%, " 20%, $Al_2(SO_4)_3$ 5%, pyrophyllite 30%, bauxite 35%	100	100	2.3	13.5
" 2%, " 20%, pyrophyllite 78%	100	100	3.1	3.5
" 50%, " 50%	100	100	2.0	3.4
" 25%, " 50%, bauxite 25%	100	100	1.8	6.7
" 25%, " 75%	100	100	2.1	5.0
" 16%, " 84%	100	100	2.3	5.7
NaF 10%, borax 90%	100	100	3.1	3.5
" 50%, " 50%	100	100	2.6	6.7
" 50%, DNOCHP 50%	100	100	1.9	5.8
" 50%, Al_2O_3 50%	85	100	3.6	14.7
" 67%, " 33%	84	100	4.3	14.1
" 50%, Anderson's clay 50%	89	100	5.2	14.8
" 67%, " 33%	88	100	3.2	14.1
" 50%, bauxite 50%	78	100	5.1	16.7
" 67%, " 33%	75	100	3.1	13.1
" 50%, talc 50%	80	100	3.2	17.0

(4) Vs. Periplaneta americana; sodium fluoride as a contact poison and rate of death; insects allowed to run 15 seconds over evenly deposited dusts: 1273

NaF Dosage (g)	♂ (mg/g)	Hrs to Death	♀ (mg/g)	Hrs to Death
2	12.9	12	7.1	24
2	10.4	24	6.0	12
2	9.3	12	5.4	12
2	4.1	24	3.8	24
2	3.4	24	3.2	24
2	mean 8.0	19.2	5.1	19.2
1	8.6	24	10.9	12
1	4.7	12	10.3	12
1	3.8	24	5.3	60
1	2.8	36	4.3	12 *
1	1.7	12	2.7	24
1	mean 4.3	21.6	6.7	24
0.5	2.3	48	1.7	132
0.5	2.0	48	1.6	72
0.5	1.6	60	1.4	132
0.5	1.5	84	1.3	72
0.5	0.9	120	1.0	132
0.5	mean 1.7	73.2	1.4	108

*In this range insects collected about as much NaF as body surface could acquire.

(5) Sodium fluoride compared with barium carbonate vs. Thermobia domestica; toxicants incorporated in baits: 2612

Compound And Concentration	% Mortality In 24 Hrs	48 Hrs	72 Hrs	96 Hrs
$BaCO_3$ 4%	27	55	75	82
NaF 4%	27	51	77	89
$BaCO_3$ 6%	27	66	78	89
NaF 6%	51	66	77	91
$BaCO_3$ 7%	24	59	79	93
NaF 7%	21	52	71	88
$BaCO_3$ 8%	43	75	91	96
NaF 8%	33	53	71	90

(6) Sodium fluoride vs. Melanoplus differentialis; oral administration:

Zone	No. Insects	Survival Time (Hrs)		Dosage ($\mu g/g$)	LD_{50}	2617
		Mean	Range			
Lethal	22	56	(32 - 84)	(0.18 - 2.61)		
Intermediate	9 dead 5 survived	105	(47 - 155)	0.11(0.07 - 0.17)*	0.11	
Sub-lethal	6			(0.04 - 0.06)		

*Mean dose which killed and mean dose which was survived.

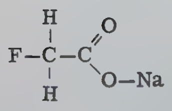
c) Comparative toxicity of sodium fluoride and other compounds for insects:
  (1) See the section titled Fluorine, Fluorides, Fluosilicates, Fluoaluminates.

d) Pharmacological, pharmacodynamic, physiological, etc.; insects:
  (1) NaF is able to penetrate the insect cuticle directly; lime enhances the toxicity as a contact poison (for 1546
  instance 2 parts NaF:1 part lime); aluminum oxide, borax, and bauxite activate NaF as a contact 1273
  poison. 2750,777
  (2) Increased the time required for food passage through gut in Periplaneta americana. 2917
  (3) Toxicity toward insects influenced by gut pH; of little toxicity to lepidopterous larvae (gut pH 9.2 - 9.7) 814
  markedly toxic to Locusta migratoria (gut pH 6.8).
  (4) Reported to inhibit insect choline esterase(s). 353
  (5) Susceptibility of Periplaneta enhanced by haemocyte blockage with carbon-black. 2172
  (6) Symptoms of poisoning in insects: Periplaneta and Blattella by contact: I) Uneasiness, irritability; 2750
  II) torpor with nervous spasms which: III) Declined gradually until death in 4 - 48 hours; symptoms
  resembled borax intoxication.
  (7) Histological effects: Disintegration and necrosis of midgut epithelium in Prodenia and Vanessa larvae 3349
  Locusta nymphs. 2510
  (8) Biochemical effects: Perfusion of muscle and fat body of Carpocapsa pomonella (larva) with NaF in- 1243
  duced decline in oxidative and glycolytic activity; the respiratory quotient was doubled. Inhibited 2750
  esterases, lipases, phosphatases; depressed catalase activity of Passalus tissue, with increase in 223,269
  dehydrogenase and phenoloxidase activity. Partially inhibited the choline esterase(s) of Apis and 2762
  Periplaneta nerve and the gut lipase of Calliptamus.
  (a) Repellency: Not repellent to houseflies at 3.5% in baits. 2815

e) Insecticidal uses; reports of effectiveness in field use:
  (1) Vs. Euxoa larva: Preferable in baits to sodium arsenite, being non-repellent. 2649
  (2) Employed successfully in baits vs. Thermobia, silverfish, moth (clothes) larvae. 2226
  (3) Vs. clothes moths: Used as a cloth impregnant. 396
  (4) Effective vs. cockroaches such as Blattella orientalis, B. germanica and Periplaneta americana. 2226
  (5) Vs. Mallophaga of the genus Damalinia (poultry lice): Useful as a dust, but largely replaced by DDT 2226
  and other insecticides.
  (6) Vs. bark beetles: Useful in wood preservation. 2815

164

SODIUM FLUOROACETATE (Sodium fluoacetate; Sodium monofluoroacetate; Compound 1080; "Ten Eighty.")



$$F{-}CH_2{-}C({=}O){-}O{-}Na$$

Molecular weight 100.033

GENERAL [Refs.: 703, 2231, 89, 2120, 2651, 704, 3228, 701, 129, 790]

Best known as a non-specific poison of extraordinary potency, and toxic hazard; used as a rodenticide and against predators in general; sodium fluoroacetate has shown itself to possess systemic insecticidal properties in treated plants for insect pests feeding thereon. Intensely poisonous to man and other vertebrates. Has been identified as the natural toxin in the "Giftblaar plant," Dichapetalum cymosum. To be used by experts only. Too generally toxic for practical systemic insecticidal use.

PHYSICAL, CHEMICAL [Refs.: 129, 89]

A colorless, odorless, tasteless, water-soluble salt, purity ca. 95%; decomposes at 200°C and should not be heated above 110° in bait preparation; very soluble in water (1 part:300 parts, 12 g/gallon); hygroscopic when exposed to air; relatively insoluble in organic solvents, and in animal and vegetable fats and oils; commercial material commonly colored with 0.5% pure nigrosine; a mild, salty, sour taste is described by some; non-corrosive to metals.

1) Formulations: Commonly sold as a compound containing 90% or more sodium fluoroacetate, colored black, to be mixed with 28 pounds food at 1 ounce in preparing baits, or 0.5 ounce per gallon in water for poisoning drinking water in indoor control of rodents.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) As judged from fatal, or near fatal, cases of human poisoning, the dangerous dose for man is ca. 0.5 - 2 mg/k. Other species vary considerably in response to sodium fluoroacetate. Primates and birds are most resistant; rodents and carnivores are most susceptible. Domestic animals fall somewhere between the two extremes. Affects the myocardium and central nervous system. 89 3228
   b) Quantitative: 3228,790,701

Animal	Route	Approximate LD_{50} (mg/k)
Dog	iv	0.1 - 0.2
Coyote	ip	0.2
Rabbit	iv	0.3
Pig	ip	0.3
Cat	ip	0.3
California Ground Squirrel	or	0.3
Black-tail Prairie Dog	or	0.3
Guinea Pig	or	0.3 - 0.4
Field Mouse	or	0.5
Bobcat	ip	0.67
Goat	im	0.7
Rat (black)	or (By tube)	1.0
Rat (Norway)	or (")	3 - 4
Monkey (Rhesus)	iv	5 - 7.5
Monkey (spider)	iv	10 - 12
Chicken	or	6 - 7
Frog	sc	1000 - 2000
Horse		1.0
Rat	or	0.2 - 7.0

2) Pharmacological, pharmacodynamic, physiological, etc.; higher animals: 89,2000
   a) Absorption:
      (1) Rapidly absorbed via gastro-intestinal tract; oral dosages approximate in toxicity sub-cutaneous, intramuscular, intraperitoneal and intravenous dosages.
      (2) Not readily absorbed through the unbroken skin.
      (3) Dusts containing sodium fluoroacetate are effectively toxic by inhalation.

b) Physiological:
  (1) Apparently acts in the body without being chemically altered.
  (2) Believed to interfere with the normal acetate metabolism in the Krebs cycle.
  (3) The metabolic action of "1080" powerfully affects the cardiovascular and nervous systems and in some species the skeletal muscles. Cardiac effects predominate in men.
  (4) CNS (especially in dog) directly affected by "1080"; in man CNS symptoms include: Epileptiform seizures with consequent severe depression.
  (5) Some cumulative action is reported and some tolerance in mouse, rat and (?) monkey.

c) Symptoms:
  (1) In all species a latent period (0.5 - 2 hrs) has been noted before symptoms.
  (2) In man (proved fatal and non-fatal cases) nausea and apprehension were first signs, followed by convulsions; after several hours *pulsus alternans* may appear, succeeded by ventricular fibrillation and death. In monkeys convulsions seize successively: Facial muscles, ear and masseter muscles then the entire musculature in violent spasms. Recovery from the muscular seizure may occur only to be followed by ventricular fibrillation and heart failure.

d) Biochemical:
  (1) In rabbit and goat: Increase in blood levels of glucose; in rabbit: Increase in lactic and pyruvic acids; in dog: Increase in acetate. Inorganic phosphate serum levels increased in goat and rabbit. Increase in plasma potassium (from 17 mg/100 cc to 25 mg/100 cc) in poisoned animals.
  (2) Fluorine values in tissues elevated in one fatal human case.

e) Pathological:
  (1) Reveals little about mode of action. Congestion of viscera, lungs (cardiac failure); focal lung hemorrhage in rat; general hemorrhage in chicken.

3) Phytotoxicity:

a) Compared with the systemic insecticides OMPA, BFPO and para-oxon sodium fluoroacetate showed a greater safety margin than the others between the insecticidal concentration and the phytocidal concentration. 701
  (1) Not phytotoxic at several times the concentration necessary for insecticidal action, but too generally toxic for practical use.

4) Systemic insecticidal action:

a) The systemic activity of sodium fluoroacetate vs. aphids is easily demonstrable. It is also toxic to aphids by contact. 701
  (1) When applied to roots of plants in sand or soil cultures the order of decreasing systemic toxicity is: Na fluoroacetate > BFPO > OMPA > para-oxon; in solution culture the order is similar, save that OMPA is = to para-oxon.
  (2) Exercises no fumigant effect, as does BFPO which yields a systemically active and toxic vapor.
  (3) Vs. aphids an extremely effective systemic insecticide, readily taken up via leaves and roots of *Vicia faba*.

b) Systemic activity vs. eggs and larvae of *Pieris brassicae*: 703
  (1) Toxic by contact to eggs and larvae of *Pieris brassicae*.
  (2) Systemically toxic to *Pieris* when taken up by roots of cabbage from solution or soil cultures or following leaf application.
  (3) Compared with others the order of systemic action is: Para-oxon > Na fluoroacetate > BFPO > OMPA.
  (4) Proved surprisingly innocuous to *Pieris* eggs and larvae as compared to para-oxon which was outstandingly toxic.

c) Systemic action vs. *Phaedon cochleariae*: 704
  (1) *Phaedon cochleariae*, by direct contact technique, showed the toxic order of several compounds to be: Para-oxon > Na fluoroacetate = dimefox > OMPA, with adults being more resistant than larvae.
  (2) The toxic order by systemic application (dipping of foliage followed by drying): Para-oxon > dimefox > Na fluoroacetate = OMPA, with the first two only yielding complete kills at practical concentrations. Na fluoroacetate (and OMPA) proved ineffective systemically vs. *Phaedon cochleariae*.
  (3) Approximate amounts needed to yield 100% kills of *Aphis*, *Pieris* and *Phaedon*:

Insecticide	Method					
	Dipping (% Conc. Solution)			Systemic (cc/3½ In Pot, 400 g Soil)		
	Aphis	Pieris (larva)	Phaedon (adult)	Aphis	Pieris	Phaedon
Na fluoroacetate	0.001	>0.1	>0.1	0.001	0.02	>0.1
OMPA	.05	> .2	>1	.02	> .04	> .1
Dimefox	.05	> .1	> .5	.002	> .02	.01
Para-oxon	.0005	.01	.01	> .04 g	.002 g	.002 g

5) Comparative toxicities for animals:

Animal	mg/k Na fluoroacetate	OMPA	Para-oxon	BFPO
Rat	or, LD$_{50}$ 0.2 - 7.0	or, LD$_{100}$ 18, sc 18	-	-
Mouse	-	-	or, LD 2	or, LD 3-5, sc 1-2

165

SODIUM FLUOSILICATE (Sodium silicofluoride; Salufer.)

Na_2SiF_6 Molecular weight 188.05

GENERAL [Refs.: 353, 129, 2120, 314, 2444, 3214, 436, 2911]

A fluorine-containing, inorganic insecticide which has been used as a dust or spray to control some insects on field crops and in baits, designed to kill such forms as cutworms, mole crickets, grasshoppers and cockroaches. Effective as a moth-proofing agent for woolen fabrics. At the present time largely superseded in the control of some insects, such as grasshoppers, by chlordane, aldrin, toxaphene. Less toxic for man, livestock, than the arsenical compounds employed similarly.

PHYSICAL, CHEMICAL [Refs.: 129, 314]

A white, crystalline, or amorphous powder; average particle size = 25 micra; m.p. at red heat (but with prior decomposition); specific gravity 2.755; soluble in water to 0.65 g/100 cc at 17°C, 1 part:150 parts cold water, 1 part:40 parts at 100°C; not compatible with calcium or lead arsenate, Bordeaux Mixture, lime, lime-sulfur, in ratios less than 1:9; coloring is required to avoid confusion with various common comestibles.

1) Formulations: Dusts at 1:2 with inert diluents; bran baits; 0.5% solution as sprays and dips vs. clothes moths.

TOXICOLOGICAL

1) Acute toxicity for higher animals:
   a) Safer than lead arsenate and sodium fluoride, than which it is less soluble. Toxicity is in direct ratio to fluorine content, fluorine being the toxic principle. Moth-proofed clothing treated with sodium fluosilicate offers no hazard. 2911 2888 353
      (1) At 900 ppm, fluorine, regardless of source whether fluoride, fluosilicate or fluoaluminate is fatal in 10 days to the rat; the solubility of the fluorine source is the determining factor, for instance calcium fluosilicate and sodium fluoaluminate yield similar death rates at 40,000 - 50,000 ppm.
      (2) Baits containing sodium fluosilicate are distasteful to stock and not readily eaten by birds. 2447
   b) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Frog	sc	MLD	400		2842
Rat	or	LD_{50}	ca. 125		1951
Rat	sc	MLD	70		2312
Guinea Pig	or	MLD	250		2842
Guinea Pig	sc	MLD	500		2842
Rabbit	or	MLD	125		2312
Rabbit	or	LD_{50}	138		1870
Rabbit	or	LD	150-200		132
Rabbit	sc	MLD	74-149		3262
Rabbit	iv	LD	6.06	Death within 2 minutes.	2101
Dog	or	LD_{50}	150		1870
Goat	or	LD	136-143		132

   c) Toxicity for rats; by catheter to stomach: 3027

Approximate Dosage (mg/k)	Sex	Result
100	♀	Normal.
200	♀	Normal.
275	♂	Sick for 3 days followed by recovery.
375	♀	Death in 3 hours.
400	♂	Death in 32 hours.
As dust on cage floor	-	Death in 36 hours.

   d) Toxicity for livestock, poultry and game:

Animal	Weight (lbs)	Administered Or Offered As	Consumed (Am't)	Result
Sheep	95	Bait with 4.6g Na fluosilicate	ca. $\frac{1}{4}$(rest refused)	Remained normal on pasture.
Sheep	95	Rolled oats with 4.6g Na fluosilicate	ca. 1 oz.	"
Sheep	146	Bran + 4.6g Na fluosilicate {In water by stomach tube)	all	"
Sheep	134	Bran + 9.1g " (")	all	"
Sheep	148	Bran + 18.2g " (")	all	"

d) Toxicity for livestock, poultry and game (Continued):

Animal	Weight (lbs)	Administered Or Offered As	Consumed (Am't)	Result
Sheep	148	Bran + 54.8g Na fluosilicate (In water by stomach tube)	all	Sick in 8 hrs; death in 18 hrs.
Sheep	95	Bran + 45.5g " (")	all	" 5 " 30 "
Sheep	105	Bran + 36.4g " (")	all	No symptoms for 5 days; anorexia 6th day; mortality 7th day.
Horse	1000	Bran + 36.4g	all	No effect.
Horse	1000	Rolled Oats 2 lbs + 36.4g Na fluosilicate	all	No effect.
		Same (7 hrs later)	half	No effect.
		Following day refused all poisoned food.		
		Rolled oats 6 lbs + 110g Na fluosilicate (5 days later)	½ lb	No effect.
Cow	1000	Bran 6 lb + 109.2 g Na fluosilicate	2 lb	No effect. Baited food later refused.
Sheep	100	½ lb bait (100 lbs Bran + 4 lbs Na fluosilicate)		No effect.
Sheep	100	1 lb bait (100 lbs Bran + 4 lbs Na fluosilicate) Bait offered 4 days later in large amounts; nibbled desultorily sans effect.		(Slight diarrhoea in 48 hrs.)
Horse (2 yrs old)		3 lbs bait (as above)	½ in 48 hrs	No effect.
Rabbit (fasting)		15 g bait (as above)	little	No effect.
Rabbit (fasting)		30 g bait (as above)	little	No effect.
Chicken (adult)		100 g bait (as above) sparingly eaten	80 g eaten next day	No effect.
Chicken (adult)		tasted		
Duck		200 g bait (as above)	50 g in 2 days	No effect. Ate ordinary food ravenously.
Quail (fasting)(adult)		50 g bait (as above)	25 g in 2 days	No effect.
Pheasant (")(")		200 g bait (as above)	ca. 50 g in 2 days	No effect.

e) Ca. 8 times less toxic for sheep than sodium arsenite. Sodium fluosilicate bran baits are distasteful to sheep, horses, cows and rabbits; not readily eaten by chickens, ducks, quail, pheasants. 2444

2) Chronic toxicity; higher animals:
   a) See the section titled Fluorine, Fluorides, Fluosilicates, Fluoaluminates.

3) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:
   a) See the section titled Fluorine, Fluorides, Fluosilicates, Fluoaluminates.

4) Phytotoxicity:
   a) Phytotoxic hazard is high; injurious to plants save under arid conditions. More hazardous than acid lead arsenate (q.v.) toward foliage. 353
      (1) Rendered more soluble by even weak acids, such as carbonic acid, with hydrolysis to yield soluble phytotoxic substances.
      (2) As a 0.5% suspension non-injurious to young orange foliage. 2649
      (3) As dust on sugar cane at 16 lbs per acre produced scorching with yield decrease. 1579
      (4) In moderate dosages burns grape foliage. 2580
      (5) Peach tree foliage markedly susceptible to injury. 2106
      (6) To 150 lbs per acre in soil: Reported to be a plant stimulant; at 300 lbs per acre in soil: No plant injury. 2103
      (7) At 1500 lbs per acre: Harmless to various blue grass species. 2027
   b) Slaked lime is reported to act as a "safener" reducing the amount of soluble fluorine and the consequent phytotoxicity. 485

5) Toxicity for insects:
   a) Considered to be a "nerve and stomach" poison. 353
   b) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Apis mellifera (adult)	or	LD_{50}	24.0 μg/bee	As fluorine element.	231
Bombyx mori (4th instar)	or	LD_{50}	100-130 μg/g		2819
Bombyx mori (4th instar)	or	LD_{50}	90 μg/g		459

   c) Comparative toxicity of sodium fluosilicate and other compounds for insects:
      (1) Also consult Fluorine, Fluorides, Fluosilicates, Fluoaluminates. 2325

(2) Mortality of caged Gryllus assimilis supplied with various toxicants in baits containing toxicant + 100 g bran + 95 - 105 cc water and other ingredients as indicated below: 2325

Toxicant	Amount (g) + Other(s)				% Mortality After		
					24 Hrs	48 Hrs	72 Hrs
Sodium fluosilicate	12	molasses	16 cc		59	86	92
"	12	"	"	+ orange	61	81	88
"	5	"	"	"	46	75	89
"	2.5	"	"	"	28	44	52
Sodium fluoride	5	"	"	"	30	66	84
Sodium arsenite	12	"	"	"	32	43	64
"	6	"	32 cc		14	28	40
"	5	"	16 "		16	26	40
"	5	"	"	+ orange	12	23	31
"	4	amyl acetate 1 drop			10	20	30
White Arsenic	12	molasses	16 cc	+ orange	22	38	63
"	5		"		8	13	32
Paris Green	6	syrup	"		20	34	40
Thallium sulfate	4	molasses	"		6	20	44

d) Pharmacological, pharmacodynamic, physiological, etc.; insects:

(1) Also consult Fluorine, Fluorides, Fluosilicates, Fluoaluminates for a general treatment.

(2) Reported to be non-repellent to Musca domestica in 1 M sucrose at 0.5%; non-repellent to Euxoa, Euproctis, Cirphis, Laphygma and Prodenia. 2226 760,1592

(3) Stated to be of little toxicity to lepidopterous larvae with gut pH at 9.2 - 9.7, but to be toxic to Locusta migratoria whose gut pH is 6.8; known to release more soluble fluorine in acid media. 814

(4) Histopathological effects: In Locusta at sufficient dosages yielded exfoliation and disintegration of midgut epithelium. No histopathological effects detected in Lymantria dispar or Pieris brassicae larvae. 2510

e) In field control of economic insects:

(1) Vs. Melanoplus differentialis and other orthoptera: Effective in baits, but less effective than BHC by 20%; chlordane at 0.5% is as effective as 6% sodium fluosilicate in wet baits. 2446

(2) Vs. Cirphis unipuncta, Laphygma frugiperda and Prodenia eridania larvae: Superior to arsenicals in sweet bran baits, because it is non-repellent. 2226

(3) Vs. Pterandrus on citrus: Effective as a sweetened bait spray. 2649

(4) Vs. Brachyrhinus spp.: 5% sodium fluosilicate in raisin-cereal baits reported as best control. 71

(5) Vs. Reticulitermes flavipes: An effective soil treatment against this termite. 1855

(6) Vs. cockroaches: Other materials such as organic insecticides have largely replaced. 353,2226

(7) Vs. fly larvae in refuse, dung heaps, latrines: Application of sodium fluosilicate reported to yield a simple control. 2166

166

SODIUM SELENATE

Na_2SeO_4 or $Na_2SeO_4 \cdot 10H_2O$ Molecular weight 188.95 or 369.11

GENERAL [Refs.: 2867, 353, 2231, 129, 2120, 851, 2310, 2084, 1625, 3118, 2893, 434, 960, 2400, 2721, 953, 2954, 2942]

Among the compounds of selenium which have been found toxic to such arthropods as mites on economic plants is sodium selenate. Other more complex seleniferous insecticides, for instance $(KNH_4S)_5Se$ and selenium containing organic phosphate compounds have been tested as acaricides and insecticides, on fruit trees and greenhouse crops. Sodium selenate and sodium selenite have demonstrated marked systemic toxicity vs. mites and aphids on plants which have received these compounds at the roots, from culture solutions containing selenium at 3 ppm. Sodium selenate is absorbed by the roots and translocated in the sap stream to the foliage and flowers of herbaceous plants. Applied, for example, to the soil (at 0.25 g per ft^2) in which carnations and chrysanthemums are growing, selenium is toxic (as sodium selenate) to certain acarines. On roses or other woody-stemmed plants it is not effective. Sodium selenate, and all seleniferous compounds, are highly poisonous to man and animals. It is not recommended at all, either on food crops or other crops, by the Department of Agriculture of the U. S. It is well-known that certain plants on seleniferous soil accumulate selenium with grave danger to animals feeding or grazing thereon. Livestock, feeding on plants containing 100 - 1000 ppm of selenium, exhibit "blind staggers" and on plants containing 25 ppm show the syndrome of chronic "alkali disease." Some insects, on the other hand, such as seed beetles (Bruchids, Chalcids) can complete their life-cycles successfully on plants high in selenium, for instance on seeds of Astragulus, containing 1475 ppm of selenium. Also acts as a root nematocide.

PHYSICAL, CHEMICAL

Colorless crystalline solid; d 3.098; soluble in cold water, to 83.4 g/100 g at 35°C.

1) Formulations: Usually applied as a water solution.

TOXICOLOGICAL

1) Toxicity for higher animals: [Refs.: 2954, 2400, 2893, 434, 960, 1759, 2897, 1624, 2268, 537, 2074, 2721, 938]
   a) Selenium poisoning occurs naturally among cattle, sheep, horses, pigs and poultry in both chronic and 2721
   acute forms. Intoxication is marked by loss of hair from mane and tail, soreness of feet as well as de- 2954
   formity, loss of condition and emaciation. In poultry, the eggs produce abnormal or weak nestlings. 1624
   Mandatory selenium limit in drinking water U. S. =0.05 ppm. Concentrations in water, thought safe for 938
   man have, over exposure periods of weeks, been toxic to fish.
   b) Selenium, in the form of sodium selenite or sodium selenate, is relatively toxic. The acute LD_{50} ip or iv varies in different laboratory animals from 1 - 15 mg/k. Selenium element (granular) is relatively non-toxic. 2433

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat	ip	MLD	13.8	As Se 5.25 - 5.75 mg/k.	1056
Rat	ip	MLD	3.25-3.5	As Se; source sodium selenite.	1056
Rabbit	or	LD_{100}	4		2889
Rabbit	iv	LD_{100}	2.5		2889
Dog	or	LD	4	As soluble selenite, selenate; quickly fatal.	2400
Rabbit	or	MLD	ca. 1.5	As sodium selenite.	2400
Cattle	or	LD	ca. 2 mg/lb	As selenium salts.	2268
Horse	or	MLD	ca. 1.5	As sodium selenite.	2721
Cow, Calf	or	MLD	4.5 - 5.0	" .	2721
Pig	or	MLD	6 - 8	" .	2721
Cattle	or	Non-Toxic	0.4-0.5 ppm	As selenium in drinking water.	2268
Goldfish	Medium	Toxic Dose	2.0 ppm	Se as sodium selenite; 8 days exposure.	2400
Goldfish	Medium	LC	2.0 ppm	Se as sodium selenite; 18-46 days exposure.	2400
Fish*	Medium	Toxic Dose	10.0 ppm	Sodium selenite; hard water; 98-144 hrs exposure.	2400
Fish*	Medium	Toxic Dose	100 ppm	" ; very soft water; 1-4 days exposure.	2400
Fish*	Medium	Toxic Dose	100 ppm	" ; hard water; 8-19.5 hrs exposure.	2400

*Constant exposure to small amounts which are not harmful in short-term may be very hazardous. 938

2) Chronic toxicity:
   a) Rats show toxic effects on diets with 3 - 40 ppm selenium; toxicity of 9 - 18 selenium in ration has been 2187
   counteracted by arsenicals in drinking water. 2268
   b) Ca. 4 ppm selenium in plants growing on seleniferous soils appears to be the tolerance limit for livestock. 2187

- c) For livestock, in foodstuffs 4 ppm is held the extreme limit; 3 ppm is a safer limit. 2187
- d) Livestock, feeding on vegetation containing to 25 ppm selenium, suffer chronic "alkali disease," with lack of vitality, hair loss, sterility, lameness, and ultimately death from anaemia or malnutrition. At 100 - 1000 ppm, in vegetation, livestock experience an acute disease, "blind staggers," with vision impairment, weakness of limbs, respiratory failure and death. 851
- e) Mild chronic selenium poisoning has been noted in men living in seleniferous regions. Selenium is found in the urine and there is exceptional incidence of intestinal disturbances, hepatomegaly, dermatitis and arthritic symptoms. 851
- f) Any soil with more than 0.5 ppm selenium constitutes a hazard to grazing livestock. 434

3) Pharmacological, pharmacodynamic, physiological etc.; higher animals: 851

- a) Upon absorption (primarily by mouth) selenium becomes generally distributed in the soft tissues.
  - (1) Particularly concentrates in liver and kidneys.
  - (2) Carried by blood; fixed in erythrocytes, albumen and globulin.
- b) 50% - 75% is excreted via urine, some in bile and via breath as $(CH_3)_2Se$.
  - (1) To 30% of ingested sodium selenite is eliminated via breath; responsible for a garlic-like odor of breath noted in selenium poisoning.
- c) Symptoms: Some symptoms are already suggested above in the chronic syndromes of "alkali disease" and "blind staggers."
  - (1) Humans, suffering from selenosis acquired in industrial operations, have shown: Gastro-intestinal disturbances, erythema, pallor, dermatitis, acute nasal and respiratory irritation, dizziness, "garlic breath" and metallic taste.
  - (2) H_2Se, as low as 0.2 ppm in air, produces definite toxic symptoms.
- d) Mechanism of biological action:
  - (1) Specific mechanism of toxicity remains essentially unknown.
  - (2) Selenate inhibits many enzyme systems, particularly those requiring sulfhydryl (SH^-).
  - (3) Arsenic partly counteracts some selenium effects.
  - (4) Particularly damaging to the liver, an effect which high protein diets and methionine (in presence of α - tocopherol) may counteract.
  - (5) BAL reduces liver damage, but enhances kidney damage; arsenic at 5 - 10 ppm in drinking water prevents chronic selenosis in animals. Bromobenzene may reduce selenium toxicity.
  - (6) In rats, chronic exposure to selenium is carcinogenic (liver).

4) Phytotoxicity:

- a) Phytotoxic to chrysanthemums at dosages of ca. 250 mg per ft^2 or more; some varieties are more susceptible than others. At 250 mg per ft^2, single application, phytotoxicity is minimal for some varieties. 953
- b) Difficult to maintain control of pests of carnations for more than a year using selenate without producing some degree of stunting (shortening of stems), especially at dosages more than 250 mg per ft^2. 953
- c) $\frac{1}{2}$ - 1 g per ft^2 caused severe damage to Gladiolus and severe injury to Schizanthus. 1075,966
- d) At 1 g per ft^2, growth was retarded, roots injured, blooming delayed in carnations; growth was normal at $\frac{1}{8}$ - $\frac{1}{2}$g per ft^2. 1075 966
- e) Wheat plants were severely damaged by sodium selenate at 30 ppm in soil. 1624
- f) Snapdragon (Antirrhinum) (some varieties) was injured at $\frac{1}{4}$g per ft^2; at $\frac{1}{2}$g per ft^2 most varieties were injured and at 1 g per ft^2 all varieties were injured. Roses were damaged by 2 ppm in soil. Chrysanthemums, in hydroponic sand culture, showed no injury at concentrations to 2 ppm. 1075 966 2355
- g) Uptake of selenium from sodium selenate by various plants:
  - (1) Selenium (ppm in dry tissue) in chrysanthemum plants treated at 250 mg per ft^2 soil; application on July 21st: 1075 966

Variety	PPM Selenium On Date Given				
	Aug. 10	Aug. 22	Sept. 10	Sept. 26	Oct. 9
Sylvanna	157	284	428	395	287
Omega	149	220	325	337	330

  - (2) Selenium in tomato foliage; nutrient solution culture with sodium selenate added: 2355

Selenium Concentration (ppm)	Selenium In Foliage (ppm; Mean)
0.5	57
1	121
1.5	165
2	196
Control Plants	39

  - (3) Selenium in foliage of stocks, roses and carnations; selenium applied as sodium selenate to the soil: 2355

Selenium Applied (ppm)	Mean Selenium (ppm) In Foliage Of			
	Stocks	Rose	Chrysanthemum	Carnation
0.5	21	8	12	-
1.0	55	13	14	-
1.5	77	26	25	-
2.0	96	35	45	23

(3) Selenium in foliage of stocks, roses and carnations (Continued):

Selenium Applied (ppm)	Mean Selenium (ppm) In Foliage Of			
	Stocks	Rose	Chrysanthemum	Carnation
2.5	-	45	-	-
4.0	-	-	-	28
6.0	-	-	-	69
8.0	-	-	-	75
10.0	-	-	-	115
Control	1	0	1	6

5) Systemic action of sodium selenate via treated plants on insects and acarines: 2355

a) Vs. Red spider mites, Tetranychus telarius:

Selenium Applied (ppm)	Mean "Population" Of Tetranychus telarius On					
	Tomato		Stocks		Carnation	
	*No. Mites	ppm Se In Leaves	*No. mites	ppm Se In Leaves	**No. Mites	ppm Se In Leaves
0.5	18; 52.7	87; 57	292	21	-	-
1.0	1; 6.2	98; 121	261	55	-	-
1.5	0; .2	121; 165	43	77	-	-
2.0	0; .7	191; 196	23	96	33	23
4.0	-	-	-	-	10	28
6.0	-	-	-	-	0	69
8.0	-	-	-	-	1	75
10.0	-	-	-	-	0	115
Control	88; 167.2	4; 39	341	1	70	6

*Mean number of mites on 2 leaves.
** " 4 " .

b) Vs. Macrosiphoniella sanborni on sodium selenate treated Chrysanthemum:

Selenium Applied To Soil	Mean No. Of Aphids (2 Leaves)	Selenium Conc. Of Leaves (ppm)
0.5	50	12
1.0	25	14
1.5	3	25
2.0	1	45
Control	24	1

6) Other comments on uses of sodium selenate as a systemic insecticide:

a) Chrysanthemums: Kept virtually free of mites, aphids, mealy bugs by treating soil once at 250 mg/ft^2 or twice at 125, 62.5, 31.25 mg/ft^2 ; phytotoxicity minimal even at 250 mg/ft^2 , although on some varieties effects were deleterious. 953

b) On carnations (3 varieties): In soil treated twice per year at 250 mg/ft^2 or 4 times per year at 62.5, 31.25, 15.6 mg/ft^2 all treatments gave some degree of pest control. 953

- (1) At the 2 higher dosages satisfactory control was had for more than 1 year.
- (2) After 1st year, only the 250 mg/ft^2 schedule (twice per year) gave essentially pest free plants.
- (3) No effect on size or number of flowers, but stem shortening at higher dosages.
- (4) At risk of some stem shortening, some varieties were maintained essentially pest free for 2 years with application of 62.5 mg/ft^2 every 3 months. One variety at 2, 4, 6, 8, 10 ppm in soil showed no deleterious effect.

c) On tomatoes: At 1 ppm in nutrient culture, tomatoes remained practically free of Tetranychus telarius. 2355

- (1) By 2 ppm growth is retarded and yield reduced.

d) On sorghum: Aphis maidis and Tetranychus telarius were controlled by 2 ppm selenium in soil; plants stunted at 5, 10, 15 ppm. 1978

e) On wheat: Aphids and mites on wheat, grown in solutions containing 3 ppm selenium, died within a few days of feeding; wheat was stunted by concentrations of more than 3 ppm. At 15 ppm in soil wheat suffered chlorosis and stunting. At 1 ppm in soil danger exists for animals fed on wheat grown upon such soils. 1625 2363

f) Control of thrips and Tetranychus telarius on greenhouse Chrysanthemum: Application to soil at 0.5 g per ft^2 yielded control. 1075

g) On Buxus: 1 g per ft^2 in water is reported effective for leaf miners, mites, and Psylla of boxwood. 129

167

STROBANE® (Terpene polychlorinates; 3960 x 14, B. F. Goodrich Chemical Co.)

$C_{10}H_{11}Cl_7$ Molecular weight approximately 380.

GENERAL [Refs.: 2231, 1953, 1777, 46]

An insecticide recently developed as the chlorination product (66% chlorine content) of a mixture of camphene and pinene. Consists of camphene, pinene and related terpene polychlorinates. Experimentally introduced for test purposes in 1951 as a promising insecticide of wide activity spectrum, to be used in control of common household insects, such as cockroaches, flies and silverfish; for insects of man and animals, such as ticks, lice, mosquitoes and certain crop insects of agricultural importance.

PHYSICAL, CHEMICAL [Refs.: 46, 1777]

Viscous, straw to amber-colored liquid; taste: Undetermined; odor: Aromatic, pine-like; $d^{25°}$ 1.638; n_D 1.582; v. p. 3×10^{-7} (0.3 millimicra) mm Hg at 20°C; non-flammable; solubility: Traces in H_2O; miscible in hydrocarbon and aromatic solvents; slightly soluble in 95% ethanol, soluble to 40% in odorless kerosene at room temperature; hydrolysis rate negligible in boiling water; stability: Slow dehydrogenation at 100°C; not stable in presence of organic bases; non-corrosive to carbon and stainless steels and tin plate. Compatible with commonly used insecticides and fungicides. Not to be long stored with alkaline materials. Technical and liquid concentrate should be stored in acid resistant vessels. Dusts should be held in cool, dry storage.

1) May be formulated as emulsifiable concentrates, wettable powders, dusts, oil solutions, aerosols, pressurized sprays. In aerosols, no aromatic solvent is needed to hold Strobane® in solution nor as an aerosol does it leave visible unsightly deposits. Tested aerosols have been found non-irritant and non-objectionable in odor. In household spray formulations a "knockdown" agent is essential in combination with Strobane®

TOXICOLOGICAL

1) Acute toxicity, higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rat (white)	or	LD_0	75	By stomach tube; 5% solution (w/v) in corn oil.	2810
Rat (")	or	LD_{50}	200		
Rat (")	or	LD_{100}	350		
Guinea Pig	or	LD_0	100		
Guinea Pig	or	LD_{50}	250		
Guinea Pig	or	LD_{100}	400		
Dog	or	LD_0	>50		46
Dog	or	LD_{50}	200		46
Dog	or	LD_{100}	350		46

a) Lethal percutaneous exposures: 2810
   (1) Groups of 15 rabbits receiving 4 applications of 5% Strobane® in corn oil over 10% of the body surface, dosages 1 cc/k, 2 cc/k, 4 cc/k:
   Results: 7/15 receiving 1cc/k dosages died at various times after last of 4 doses.
   8/15 receiving 2cc/k died; 1 after 2nd, 1 after 3rd, rest up to 30 days after final dose.
   12/15 receiving 4cc/k died at various intervals up to 34 days after final dose.
   9/15 receiving 4cc/k corn oil alone died at intervals to 12 days after final dose.
   (2) All treated animals were irritable and preconvulsive in behavior. No gross pathology and no consistent histopathology was attributable to treatment.
   (3) Strobane® in corn oil, white oil, paraffin oil, Ultrasene or deobase as 5% solution in repeated cutaneous exposures to 1, 2, 4 cc/k is to be considered toxic.

b) Acute exposure to pure Strobane® by cutaneous application: 2810
   (1) Rabbits, in groups of 5 exposed to 2, 3, 4, 5 cc/k dosages on the shaved skin bandaged for 1 week after treatment.
   Results: No mortalities, but at all dosages some degree of skin ulceration or inflammation.
   (2) Single doses of Strobane® , 5% solutions w/v in Ultrasene or Sonneborn Oil #51, at 5cc/k on shaven skin (bandaged) yielded no fatalities; ulceration and inflammation with Ultrasene solution, no damage with Sonneborn Oil #51 solution.

c) Exposure of rats to aerosol vapors 10 seconds/10 minutes over 8 hour periods, corresponding to continuous inhalation for 8 hours of 20 mg Strobane® /ft³: 2810
   (1) Results: No evidence of intoxication; transient lack of desire for food and water.

2) Chronic toxicity for higher animals:

a) Strobane® in the diet; rats on diets with 50 ppm ($\frac{1}{20}$ LD$_0$), 100 ppm ($\frac{1}{10}$ LD$_0$), 500 ppm ($\frac{1}{2}$ LD$_0$), 5 of each group autopsied at 2, 4, 6 months: 2810

(1) Results: Normal weight increase; no gross pathology; no consistent histopathology attributable to treatment.

b) Highest dosage fed daily to rats without gross effects over 2 year period: 500 ppm. 46

c) Chronic aerosol exposures, inhalation: 6 hr/da each day for 4 months at 2.5, 1.25, 0.62 g per 12 ft^3. 2810

(1) Result: Normal weight increase; no gross pathology; no consistent histopathology attributable to treatment.

d) Sub-acute cutaneous exposure:

(1) Groups, 10 rabbits, exposed to applications of 1 cc and 2 cc of 1% Strobane® solutions in white oil (w/v) daily, 5 days per week, for 90 days: 2810

(2) Results: At 1 cc no deaths.
At 2 cc, 2/10 died; one at end of 7, 1 at end of 35 doses.
At 4cc/k white oil alone 4/10 died; 1 after 7, 1 after 22, 1 after 23, 1 after 24 doses.

(3) Dermatitis, less in the oil controls than in Strobane® exposed animals, with pronounced epithelial hyperplasia in animals exposed to 2cc/k dosages.

3) Cumulative toxicity: 2810

a) Relative lack of accumulation in body is suggested by innocuousness of 500 ppm chronically taken in diet, in contrast to toxicity (rat) of single oral 75 mg/k dosages.

b) Effect typical for chlorinated terpenes, of which small quantities may be toxic in single dose, while repeated small quantities taken for long periods are tolerated.

4) Summary:

a) 500 ppm = highest level producing no gross effects when fed daily to rats over a 2 year period. 46

b) Application to 10% of the body surface (of rabbits) of doses up to 5 cc yielded no mortalities. 46

c) Application daily over a 90 day period to 10% of the body surface (of rabbits) of 2 cc/k of 1% solution of Strobane® produced no pathological changes. 46

d) In Man: No primary irritation and no sensitization responses were noted in 50 human subjects given 15 successive skin applications followed by a 16th after a two week interval. 46

5) Pharmacological and other biological considerations:

a) For man no data are available. 46

b) Essentially, death of experimental animals exposed to Strobane® by various portals of entry has been laid to damage of the central nervous system, liver and kidneys. 46

c) Treatment of intoxication: No specific antidote; treatment symptomatic supportive as in other chlorinated hydrocarbon intoxications. Antispasmodics may control convulsions. Skin decontamination should be prompt in case of spills or other exposure. If ingested, vomiting should be induced and, if necessary, gastric lavage performed; narcotics are contraindicated. 46

6) Phytotoxicity:

a) Damaging and toxic to certain of the Cucurbitaceae, to prunes, and (possibly) to peaches and other stone fruits. 46

b) Persistence and effect in the soil as yet undetermined.

7) Wild life hazards:

a) Strobane® appeared somewhat less toxic for quail than DDT, in preliminary studies. 780,781

(1) Diets with 0.005% Strobane® had little effect on growth or survival of quail chicks. Some depression of growth was possible during first 5 experimental weeks, but individual variations within control and experimental animals cast doubt on the significance.

(2) Young quail probably more susceptible than adults to prolonged Strobane® ingestion.

(3) During winter, when quail and pheasant dietary requirements are less critical, satisfactory survival occurred in both bird varieties at feeding levels to 50 ppm over 162 day periods.

(4) Strobane®, at 100 ppm in diet of breeding quail, gave no evident effect on egg production, % fertility or hatchability. Chick viability of birds hatched from eggs of treated birds was reduced, and the reduction was particularly marked among chicks whose parents received Strobane® throughout growth, winter and reproduction periods.

(5) Among pheasants, Strobane® at 50 ppm seemed to depress viability of chicks hatching from eggs of treated parents.

b) Toxicity of Strobane® for young and adult quail and young pheasants; feeding tests. 780,781

Bird	Age At Start (days)	Test Length (days)	Level Fed		Consumed (mg/k)		Mortality (%)	Survival (days)	Number Of Birds
			%	ppm	daily	total			
Quail (adult)	-	-	0.05	500	38.0	3195	28.6	84	8
" "	-	-	.025	250	10.6	890	25.0	84	8
" "	-	-	.01	100	11.3	945	0	84	8
" " (control)	-	-	-	-	-	-	4.1	154	96
" (young)	1	6	.1	-	77.2	420	100	-	20
" "	1	9	.05	-	27.8	250	100	-	20
" "	1	120	.005	-	5.3	620	20	-	20

b) Toxicity of Strobane® for young and adult quail and young pheasants; feeding tests (Continued):

Bird	Age At Start (days)	Test Length (days)	Level Fed %	Level Fed ppm	Consumed (mg/k) daily	Consumed (mg/k) total	Mortality (%)	Survival (days)	Number Of Birds
Quail (young)(control)	1	120	-	-	-	-	28.5	-	200
Pheasant (young)	1	103	.005	-	4.3	448	25	-	20
" (control)	1	120	-	-	-	-	31.5	-	200

c) Effect of Strobane® on growth and survival of Quail: 780,781

Test Length (wk)	Controls Survival (%)	Controls Wgt (g)	Strobane® .005% In Diet Survival (%)	Strobane® .005% In Diet Wgt (g)
1	96	16	97	13
2	96	26	97	23
3	96	50	91	42
4	90	70	78	58
5	82	90	75	76
6	78	110	75	97
7	78	124	75	114
8	78	130	75	130
9	78	155	75	142
10	78	163	75	156

d) Effects of Strobane® on reproduction of Quail and Pheasant: 780,781

Bird	Level Fed (ppm) During Winter	Level Fed (ppm) During Reproduction	Mortality (%)	Eggs (average/hen)	Fertile (%)	Hatchability (%)	% Chicks Surviving At 2 Wks	% Chicks Surviving At 6 Wks
Quail	50	0	0	69	86.6	91.9	100	85.0
"	50	50	0	51	90.5	71.5	63.6	50.0
"	0	100	0	36	76.8	73.0	100	62.5
" (control)	0	0	6.25	52	89.0	83.9	88.9	83.3
Pheasant	50	50	0	37	79.0	51.9	75.0	62.5
" (control)	0	0	0	48	86.6	57.4	94.8	89.7

8) Toxicity for insects:

a) Tests purely preliminary and indicative only: 1777

(1) As direct spray for various cockroaches:

Concentration (%)	Blatella germanica (4th Instar) % Dead or Moribund At 24 Hrs	Blatella germanica (4th Instar) % Dead or Moribund At 48 Hrs	Periplaneta americana (nymphs) % Dead or Moribund At 24 Hrs	Periplaneta americana (nymphs) % Dead or Moribund At 48 Hrs	Blatta orientalis (nymphs) % Dead or Moribund At 24 Hrs	Blatta orientalis (nymphs) % Dead or Moribund At 48 Hrs
0.05	20	27	13	26	13	6
.125	20	30	0	6	6	20
.250	15	40	26	33	0	0
.500	30	43	0	6	46	46
1.0	20	37	6	20	13	20
2.0	66	80	26	40	26	26
OTI*	23	43	53	66	40	40

*= Official Test Insecticide; Pyrethrins 100 mg/100 cc

(2) Musca domestica (large groups, 4 replicates): Strobane® as sprays, in combination with "knock-down" toxicants; Peet-Grady Tests:

Companion Toxicant Pyrethrins (%) w/w	Strobane® (By Wgt) %	KD (%) In 3 Min	KD (%) In 10 Min	Mortality (%) In 24 Hrs	OTI Difference	Number Of Flies
.05	.25	-	75.5	69.7	+ 18.6	-
.05	.5	-	89.0	87.3	+ 37.3	-
.05	1.0	-	89.5	89.5	+ 35.5	-
OTI		-	95.3		-	-
.075	.25	-	82.5	75.0	+ 23.9	-
.075	.5	-	92.6	88.9	+ 36.9	-
.075	1.0	-	93.7	93.7	+ 39.6	-
OTI		-	95.9		-	-
.1	.25	-	93.8	91.7	+ 38.1	-
.1	.5	-	94.5	94.3	+ 44.8	
.1	1.0	-	95.5	94.6	+ 45.1	-

(2) Musca domestica (large groups, 4 replicates) (Continued):

Companion Toxicant Pyrethrins (%) w/w	Strobane® (By Wgt) %	KD (%) In 3 Min	KD (%) In 10 Min	Mortality (%) In 24 Hrs	OTI Difference	Number Of Flies
OTI		-	95.2		-	-
.125	.25	-	94.2	86.6	+ 36.6	-
.125	.5	-	97.5	95.2	+ 43.2	-
.125	1.0	-	95.1	94.0	+ 40.4	-
OTI		-	94.6		-	-
.063	-	87.7	93.4	26.6	- 7.4	-
.063	.25	86.8	93.0	67.1	+ 33.1	-
.063	.5	88.4	93.9	85.0	+ 51.0	-
OTI		93.7	96.3	34.0	-	-
Lethane 384 v/v (%)		-				-
1.5	1.0	-	98.0	96.5	+ 49.5	-
1.5	.5	-	96.0	69.0	+ 23.0	-
1.5	.25	-	97.0	55.0	+ 8.0	-
OTI		-	96.0	47.0	-	-
Thanite (%)v/v						
1.5	0.25	-	87.7	42.5	+ 10.8	1155
2.0	0.25	-	90.7	55.1	+ 23.4	1246
2.5	0.25	-	94.1	54.7	+ 23.0	1383
3.0	0.25	-	93.5	61.0	+ 29.3	1115
OTI	-	-	92.0	31.7	-	2606
1.5	0.5	-	92.0	60.9	+ 21.2	1593
2.0	0.5	-	94.5	68.0	+ 28.3	1577
2.5	0.5	-	95.4	64.8	+ 25.1	1556
3.0	0.5	-	95.0	74.7	+ 35.0	1827
OTI	-	-	91.0	39.7	-	3452
1.5	1.0	-	88.5	69.9	+ 36.1	1497
2.0	1.0	-	91.3	74.7	+ 40.9	1322
2.5	1.0	-	91.7	73.4	+ 39.6	1456
3.0	1.0	-	94.7	76.0	+ 42.2	1445
OTI	-	-	90.5	33.8	-	2914

(3) Peet Grady Tests; vs. Musca domestica; various formulations:

Substance (mg/100 cc)	Tests No.	% KD In 3 Min	% KD In 5 Min	% KD In 10 Min	% Mortality KD Kill	% Mortality Total Kill
Pyrethrins:20, Piperonyl butoxide:160	6	38	52	90	82	84
Pyrethrins:20, Butoxide:160, Strobane:500	5	31	42	89	89	90
Allethrin:45, Butoxide:225, Strobane:500	6	36	47	86	86	88
Strobane:500	6	3	6	9	-	-
OTI (Pyrethrins 100 mg)	6	47	58	92	46	-

(4) Vs. Blattella germanica adult ♂♂ by WFA method; replicates 3; 15 roaches per test:

Strobane® (%)	Dosage (cc)	% Mortality (48 Hrs)
.5	.7	64
1.0	.7	49
3.0	.7	100
5.0	.7	100
OTI	-	82

(5) Tests against certain other arthropods; Dosage 12cc; Exposure 15 minutes; Strobane® concentration = 2.5%:

Arthropod	No.	No. (24 Hrs) Dead	No. (24 Hrs) Dying	No. (48 Hrs) Dead	No. (48 Hrs) Dying	% Dead or Moribund At 24 Hrs	% Dead or Moribund At 48 Hrs
Silverfish	30	28	2	29	1	100	100
House spider	10	10	0	10	0	100	100
Bedbug	33	14		33		40	100

(6) Various results of aerosol tests using Strobane® in the formulations are given in the paper cited; these are not quoted because the complete nature of the formulations is not specified.

(7) Comparison of the effect of Strobane® and other insecticides, used as dusts, on certain beneficial insects: 1404

a) Adult insects placed on plants previously dusted by the vacuum dusting method.

Insecticide And Dust Concentration		% Mortality 24 Hrs Of Collops vittatus	% Mortality 24 Hrs Of Hippodamia convergens	% Mortality 24 Hrs Of Coleomegilla maculata
Strobane®	5%	10	18	12
DDT	5%	38	6	32

(7) a) Adult insects placed on plants previously dusted by the vacuum dusting method (Continued):

Insecticide And Dust Concentration		% Mortality 24 Hrs Of Collops vittatus	Hippodamia convergens	Coleomegilla maculata
Perthane	5%	23	6	12
Heptachlor	2.5%	41	30	38
Toxaphene®	10%	32	12	36
Endrin	1%	27	10	18
Dieldrin	2%	36	4	24
Parathion	2%	65	78	98
Malathion	5%	47	90	100
Chlorothion®	5%	64	82	100
Diazinon	4%	37	66	100
Control		11	4	0
Lowest Significant Difference	5% level	20	24	26

(8) Comparison of Strobane® and other insecticides, used as baits in sugar and molasses solutions for Musca domestica; Laboratory Tests: 1915

Insecticide And Concentration		% Down Or Dead At 30 Min	1 Hr	24 Hrs
Strobane®	1%	10	36	96
Aldrin	1%	20	76	100
BHC	1%	43	76	100
Dipterex	0.1%	54.5	56.5	100
Chlordane	1%	10	20	100
Chlorobenzilate	1%	0	0	60
DDT	1%	30	44	98
CS-708	1%	13	20	80
Diazinon	1%	23	36	96
Dieldrin	1%	20	66	100
Heptachlor	1%	6	48	100
Lindane	1%	3	6	100
Lethane 384®	1%	0	0	0
Malathion	1%	43	56	93
Metacide	1%	23	23	100
Methoxychlor	2%	23	20	93
NPD	1%	36	40	90
Parathion	1%	13	13	90
TEPP	.5%	53	56	100
Toxaphene®	1%	40	56	100
Borax (saturation)		0	0	33
Boric acid	.63%	3	3	50
Copper sulfate	2%	0	0	36
Formalin	2%	16	16	30
Cryolite	1%	0	0	0
Sodium fluoride	2.5%	0	0	66
Rotenone	1.3%	0	0	50

(9) Strobane®, compared with other insecticides in the control of lice on livestock and poultry; as emulsions, wettable powders, dips: 2862

Insecticide	Spot treatments vs. Haematopinus eurysternus On Cattle: Concentration (%)	% Kill 24, 48 Hrs	Weeks Effective	Dips For Bovicola caprae, B. limbatus On Goats: Concentration (%)	% Kill 24, 48 Hrs	Infestation After 4 Weeks
Strobane®	.5	100	4	.2	100	0
"				.1	100	0
DDT	.5	100	4	0.25	100	0
"	.25	100	3			
Toxaphene®	.5	100	4			
Endrin	.05				100	0
Isodrin	.05				100	0
Malathion	.5	100	2	.25	100	0
"	.05	100	1	.1	100	0
"				.05	100	0
"				.025	100	0
Parathion	.05	100	3			
"	.01	100	3			
"	.005	25	0			

(9) Strobane®, compared with other insecticides in the control of lice on livestock and poultry; as emulsions, wettable powders, dips (Continued): 2862

Insecticide	Spot treatments vs. Haematopinus eurysternus On Cattle: Concentration (%)	% Kill 24, 48 Hrs	Weeks Effective	Dips For Bovicola caprae, B. limbatus On Goats: Concentration (%)	% Kill 24, 48 Hrs	Infestation After 4 Weeks
Chlorthion®	.25	100	1	.002	100	0
Dipterex	.25	100	1	.1	100	light
"	.1	100	0	.05	100	"
"				.025	100	"
"				.01	100	"
"				.002	100	"
Bayer 21/199	.25	100	2	.002	100	0
"	.2	100	2			
"	.1	100	1			
"	.05	100	1			
Diazinon	.25	100	2	.05	100	0
"	.1	100	2	.025	100	0
"	.05	100	1	.05	100	0
"	.01	95	1	.005	100	light
"	.005	25	1			
"	.002	5	1			
Bayer 21/200				.002	25	light
Pyrazinon	.25	100	3			
EPN®	.25	100	1	.002	100	0
"	.01	100	1			
"	.005	100	1			
"	.002	25	0			
Tetrapropyl dithiopyrophosphate	.05	100	1			
2-Pivalyl indanedione	1.0	100	3			
	.5	100	2			
	.25	100	2			
	.1	100	2			
	.05	100	2			

On chickens vs. Eomenacanthus stramineus the following insecticides as dusts with kaolin as diluent:

Strobane®
DDT
Toxaphene®
Chlordane
Methoxychlor
} 5% dusts

TDE
Lindane
Malathion
Diazinon
} 1% dusts

} Gave Complete Control Of Original Infestation } All Effective For 4 Wks Except For { Methoxychlor Lindane Malathion Diazinon } Which Permitted Light Reinfestation In 2 - 4 Weeks.

168

SULFUR (Sulphur; Flowers of Sulfur (=Sublimed Sulfur); Flour Sulfur (=Ground "Rock" Sulfur); Precipitated Sulfur; Brimstone.)

S (symbol) Atomic weight 32.066; atomic number 16; valence 2, 4, 6.

GENERAL (Also consult Lime-Sulfur) [Refs.: 484, 353, 2815, 1059, 757, 129, 2120, 1801, 1217]

A long-used, selective acaricide and insecticide. Sulfur is also, in many situations, an effective fungicide. Under certain conditions, sulfur is used for control of potato leaf hopper, cotton fleahopper, tomato psyllid and plant bugs. The insecticidal efficiency of sulfur depends on its fineness. The average particle size of commercial sulfur ranges from 5 - 25 micra in diameter.

PHYSICAL, CHEMICAL [Refs.: 2815, 129, 2120, 2221, 353, 3044]

Sulfur occurs in various physical states but for this purpose is to be considered as a fine; yellow powder (flowers of sulfur refers to small crystals formed by the condensation of distilled sulfur vapors); m.p. 115°C (melting to a yellow mobile liquid which darkens and becomes viscous at 160°C); m.p. differs for various allotropic forms, for instance, rhombic sulfur m.p. 112.8°C, monoclinic sulfur m.p. 119°C; d (rhombic) 2.07; b.p. 444.6°C; n_D (rhombic) 1.957; v.p. 3.9×10^{-6} at 30.4°C, 0.00002 mm Hg at 20°C; 6 times more volatile at 30° - 35° than at 24° - 26°C, 80 times more volatile at 40° - 45°C than at 24° - 26°C; insoluble in water; slightly soluble in alcohol, ether, petroleum oils; crystals soluble in carbon disulfide; amorphous form insoluble in carbon disulfide; soluble in benzene, toluene; flammable; no odor or taste; inert and generally compatible with most pest control materials; fire hazard is marked under conditions of commercial sulfur-grinding; subject to slow hydrolysis by water.

1) Formulations: Elemental sulfur is available in dry form treated or untreated with conditioners and wetting agents which render it suitable for spraying or dusting; generally, more effective at the smaller particle sizes. Flotation (and Grinrod process sulfurs) have particle sizes of ca. 5 micra diameter or less, other sulfurs (group 2) have particle diameters ca. 8 micra or less; group 3 includes conventional milled forms of particle diameter less than 12 micra; group 4 refers to coarser products; group 5 means unclassified as to particle size.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Generally non-toxic for man and mammals; may, when taken orally, have a laxative effect possibly due 129,851
   to formation of hydrogen sulfide in the intestinal tract. No dermal toxicity. Indeed, as a microcrystalline 2120
   powder (precipitated sulfur U.S.P.) sulfur is a time-honored fungicide, incorporated in 1 - 10% concentra- 2221
   tions in lotions, ointments and powders. Higher concentrations may irritate inflamed skin but sulfur preparations, on the whole, are well tolerated. Anti-fungal effect probably dependant on formation of a reduction product, such as H_2S.
   b) Toxicity of colloidal sulfur for fish: 2954

Fish	Route	Dose	Dosage	Remarks	
Carassius auratus	Medium	LC	1600 ppm	In tap water; exposure 3.5-5.25 hours.	939
Carassius auratus	Medium	LC	2100 ppm	In tap water; exposure 48-71 minutes.	939
Carassius auratus	Medium	LC	16,000 ppm	Death in 5 hours.	1437
Carassius auratus	Medium	LC	200,000 ppm	Death in less than 1 hour.	1437
Carassius auratus	Medium	Probable Threshold	10-80 ppm		1437

2) Phytotoxicity:
   a) Generally not phytotoxic or hazardous to plants save in the case of Cucurbitaceae and other such "sulfur- 353
   shy" or sensitive plants. 129,2120
   b) May be particularly injurious at high temperatures. 353,129
      (1) A marked decline in photosynthetic activity has been noted in apple tree leaves treated with sulfur. 1639

3) Toxicity for insects; acarines:
   a) Toxic action vs. acarines and small insects is believed due to reduction of sulfur to H_2S which is very toxic. 353
   b) Exercises a repellent action upon some insects, for example, on egg-depositing Paratrioza cockerelli, 353
   Lyctus spp., etc.
   c) A paralysis of the ovipositor has been noted in Lyctus spp. on sulfured wood. A paralysis of the antennae, 1018
   with death in 24 hrs. has been described in Metaphycus helvolus exposed to sulfur.

d) Stomach toxicity of sulfur has been remarked for: Malacosoma americanum (larva), Prodenia eridania 2070
(larva), Peridroma margaritosa (larva), Laphygma frugiperda (larva). Larvae of Epilachna varivestis and 787
Leptinotarsa decemlineata were not affected by sulfur. Non-toxic (at high oral doses) to Catalpa sphinx
moth larva, salt marsh caterpillar, fall web worm.

(1) In Prodenia eridania, lethal doses led, in 12 hrs., to inactivation and constipation; in 24 hrs. to regurgitation, followed by death during the second day and later by blackening of parts of the turgid body of the dead larva.

e) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Periplaneta americana (adult)	inj.	LD_0	500 μg/g	As wettable sulfur, "micronized."	2219
Periplaneta americana (")	inj.	LD_{50} ca.	900 μg/g	" , " .	2219
Periplaneta americana (")	inj.	LD_{100} ca.	1600 μg/g	" , " .	2219
Pieris brassicae (larva)	or	MLD	29.6 mg/insect		1680

(1) Sulfur as a stomach insecticide; ingested from dusted leaves by larvae of Lepidoptera: 787

Sulfur Sample	Insect		Deposit (mg/cm²)	Amount Consumed (mg)	% Mortality
Dusting Sulfur (A)	Prodenia eridania	(5th instar)	0.108	1.0	64
"	"	"	0.368	1.5	100
"	"	"	0.812	1.5	100
" (B)	"	"	0.1	1.0	71
Flowers of Sulfur	"	"	0.128	1.0	75
Wettable Sulfur	"	"	0.116	1.0	85
"	"	"	0.089	1.0	92
"	"	"	0.202	1.2	96
Dusting Sulfur (A)	Lycophotia margaritosa	(5th instar)	0.096	1.0	0
"	"	"	0.208	1.2	46
"	"	"	0.368	1.5	83

(2) Sulfur as a stomach poison; applied as a spray of wettable sulfur to leaves: 787

Concentration Of Spray (g/liter)	Insect		Deposit (mg/cm²)	Average Consumed Per Larva (mg)	% Mortality
20	Prodenia eridania	(5th instar)	0.05	0.8	2.5
40	"	"	0.1	1.1	41
80	"	"	0.2	1.2	94
120	"	"	0.3	1.5	100
80	Laphygma frugiperda	(5th instar)	0.16	1.5	20

(3) Sulfur vs. various acarines on greenhouse plants: 2869

Form	Acarine	% Mortality For			
		Adults	Quiescents	Larvae	Eggs
Sulfur Dust	Tarsonemus latus	100	95.8	100	0
"	Tarsonemus pallidus	57.1	48.7	54.5	0
Sulfur Vapor	Tarsonemus latus	100	100	100	0
"	Tarsonemus pallidus	9	0	0	0

(4) Sulfur in various forms vs. Petrobia tritici on onion plants; applied at 15 lbs per 200 gallons spray per acre; 86.1 mites per plant = average starting "population": 1734

Treatment	Average No. Mites Per Plant 4 Days After Treatment	Average No. Mites Per Plant 11 Days After Treatment
Sulfur (300 mesh, conditioned)	4.7	0.3
Sulfur + Cubé 9:1	13.1	0.3
Sulfur + Powco "A" 8.5:1	15.3	1.1
Sulfur Wettable 10/50 Spray	101.0	40.2
Control	126.0	330.1

f) Toxicity for beneficial insects: 2650
(1) Non-toxic for Apis mellifera. 2815
(2) Detrimental to many predators of orchard acarines and to some predators of Lepidosaphes ulmi. 2039,2038

g) In field control of economic insects, acarines:
(1) Vs. Lygus pratensis, L. campestris: Inadequate control. 33
(2) Vs. Aphis gossypii: Useful control for developed infestations. 1655
(3) Vs. Macrosiphum pisi: With DDT in 4% dusts more effective than nicotine or thiocyanates. 1910
(4) Vs. Frankliniella cephalica: On citrus may be controlled by sulfur. 353
(5) Vs. Cotton insects: As a dust diluent for toxaphene serves to check the upsurge of Tetranychus infestations due to the action of toxaphene on predators. 353

(6) Vs. *Anthonomus signatus*: Formerly used to combat. 543
(7) Vs. *Sarcoptes scabiei*: Used in ointments to control the pest on human subjects. 2226
(8) Vs. *Sarcoptes scabiei*: Chorioptes bovis: 3% wettable sulfur sprays on cattle granted 8 months protection. 2789
(9) Vs. *Trombicula irritans*: 60 lbs per acre were required to yield useful control. 353
(10) Vs. *Mallophaga* of livestock: Replaced by other insecticides. 353
(11) Vs. *Hypoderma bovis*, *H. lineatum* on cattle: Used with rotenone in control of. 1086,2918

h) For uses as a summer acaricide consult Refs. 440, 2145, 2226, 3000, 3235.

169

SULFUR DIOXIDE (Sulfurous anhydride; Sulfurous oxide)

SO_2 Molecular weight 54.07

GENERAL [Refs.: 353, 2815, 1059, 757, 484, 539, 990, 991, 2164, 2758, 2763, 2954]

An insecticidal gas which, under particular circumstances, for example fumigation for bed bugs, *Cimex lectularius*, may be used effectively. Fumigation with SO_2 , achieved by the burning of sulfur, is an ancient method mentioned by Homer as "pest-averting sulfur" and "divine and purifying fumigation." The use of sulfur dioxide is attended by certain decided disadvantages apart from its intense phytotoxicity, namely it has an unfavorable bleaching and tarnishing effect; it damages wheat flour with regard to baking quality and it affects the germination capacity of seeds. However, in the fumigation of empty railroad cars and other such spaces to control such insects as *Oryzaephilus surinamensis* and *Ephestia cautella* SO_2 is very effective.

PHYSICAL, CHEMICAL [Refs.: 539, 2815, 2221, 353, 2048, 1294, 851, 2954]

A colorless, non-inflammable gas of a strong, choking, suffocating odor and acid taste which in the presence of water forms sulfurous acid; m.p. -72.7°C; b.p. —10°C; liquid density = 1.434; gas density ≐ 2.2 (air = 1); v.p. >760 mm Hg at 25°C, a gas at ordinary temperatures; vapor saturation at 25°C = 2670 mg/liter; highly soluble in water, 22.8 g/100 cc at 0°C; corrosive in the presence of moisture; tarnishes metals; bleaches wall papers and fabrics; 1 mg/l = 382 ppm; 1 ppm = 0.00262 mg/l.

1) Formulations: May be produced by burning sulfur or sulfur candles; under pressure as liquid in commercial gas cylinders. When sulfur is burned ca. 10% sulfur trioxide is also formed.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Highly toxic to human beings and animals. However, vapors (even at low concentration) are so irritating and self-warning as to minimize greatly the toxic hazard where exit or escape is available. 539 851
      (1) Laboratory animals can tolerate 33 ppm indefinitely. 3259
      (2) Exposure to 500 ppm for 1 hour is dangerous, but 200 ppm is intolerable and will drive a man out. Maximum tolerable concentration 60 minutes = 0.13 mg/l, 8 hours = 0.02 mg/l. 1665
   b) Particularly toxic to the eyes and pulmonary epithelium. Use as a heat-transfer agent in refrigerators is being discontinued because of hazard from leaks. No specific antidote exists. 851
   c) A general protoplasmic poison, precipitating and denaturizing proteins by mineral acid formation. An irritant, as opposed to a narcotic, poison. 10 ppm in tap water caused trout to float helplessly within 10 minutes. 939
   d) Quantitative:

Animal	Route	Dose	Dosage		Remarks	
			mg/l	ppm		
Frog	inh	LC	2.4 - 3.0	820 - 1150	Death after several hrs exposure.	1040
Frog	inh	LC	2.6	1000	Continuous exposure 15 - 20 minutes.	1040
Mouse	inh	LC	1.6	600	" 5 hrs.	1040
Mouse	inh	LC	2.0	800	" 20 minutes.	1040
Rat	inh	LC	2.6	1000	" 20 minutes.	1040
Rat	inh	LC	0.1% v/v		2 - 4 hrs. exposure.	3308
Rat	inh	LC	0.2% v/v		1 - 2 hrs. exposure.	3308
Rat	inh	LC	1.3% v/v		1 hr or less exposure time.	3308
Sunfish	Medium	LC		16-19	Death in 1 hr.	939
Trout	Medium	LC		5	Death in 1 hr.	940
Fish	Medium	LC		0.5	As sulfurous acid.	173

2) Phytotoxicity: [Refs.: 3398, 3086, 2154, 757, 2249]
   a) Very toxic to plants. Delays germination of seeds. At 1000 ppm does leaf injury to tomato plants at 1.5 minutes exposure, stem injury at 22 minutes exposure.
   b) Highly toxic to pathogenic fungi. Reduces the spoilage of fresh fruits by its toxic action on molds and mold fungi.
   c) Brings about necrosis of leaves, defoliation, shedding of flowers. Causes premature death of buds and flowers of begonias, Calanthes and other orchids.
   d) There is an abundant "literature" on the toxic effects of SO_2 (in coal smoke and other smokes) on vegetation.
   e) Toxicity of SO_2 for plants is enhanced by a relatively high temperature and humidity.
      (1) At 1 ppm and 1 - 7 hrs. exposure injurious to most plants; orchids proved comparatively resistant.

3) Toxicity for insects:
   a) Readily absorbed by the insect body being highly water soluble. 353
   b) In case of Cimex lectularius the egg is more resistant than any stage, with the greatest resistance being during first half of the incubation period, followed by a gradual decline in resistance thereafter. Nymphs are more resistant than adults, and starved nymphs are more resistant than recently fed nymphs. 1232
      (1) Resistance of long-starved nymphs may be as high as that of eggs.
   c) Symptoms of SO_2 intoxication in Melanoplus nymphs: Irritability, intensified grooming movements, ataxia, 3259
   paralysis of posterior legs. 2749
      (1) The absorbed vapor enters into stable combination with and precipitates the tissue proteins. 412
   d) In Sitophilus granarius narcosis may not intervene to end the stage of irritation and hyperactivity until at least an hour has passed. 412
   e) Order of susceptibility in Cimex reported as: Young nymph > adult > old nymph > egg. 2003
   f) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Cimex lectularius	Fumig	LC_{50}	6.7 mg/l		417
Ephestia kühniella	Fumig	LC_{50}	16 mg/l		417
Sitophilus granarius	Fumig	LC_{50}	10 mg/l		417
Sitophilus granarius	Fumig	LC_{50}	5.7 mg/l	5 hrs exposure at 25°C, empty flask.	156,2816
Sitophilus granarius	Fumig	LC_{99}	11.3 mg/l	" " "	156,2816
Sitophilus granarius	Fumig	LC_{100}	8.3 mg/l	" 20°C, " .	412
Sitophilus oryzae	Fumig	LC_{50}	31 mg/l		417
Sitophilus oryzae	Fumig	LC_{50}	17.0 mg/l	" 25°C, " .	156,2816
Sitophilus oryzae	Fumig	LC_{99}	46.9 mg/l	" " "	156,2816
Sitophilus oryzae	Fumig	LC_{100}	10.8 mg/l	" 20°C, " .	412
Tineola bisselliella	Fumig	LC_{50}	24 mg/l		417
Tribolium castaneum	Fumig	LC_{50}	17 mg/l		417
Tribolium castaneum	Fumig	LC_{100}	9.7 mg/l	5 hrs exposure at 20°C, empty flask.	412
Tribolium confusum	Fumig	LC_{50}	5.7 mg/l	" 25°C, " .	156,2816
Tribolium confusum	Fumig	LC_{99}	10.7 mg/l	" " " .	156,2816
Ephestia cautella Oryzaephilus surinamensis	Fumig	LC	2.8-3.0% w/w	1 hr exposure both at top and bottom of empty RR car.	353
Ephestia cautella Oryzaephilus surinamensis	Fumig	LC	0.8-2.6% w/w	2 hr exposure both at top and bottom of empty RR car.	353

(1) SO_2; mg/l required to kill various stages of Cimex lectularius at 23°C, 60% Rel. Humidity, 2.5 hrs. exposure: 1232

Stage	Average No. In Each Of 10 Tests	mg/l For 100% Mortality
Egg (0 - 2 days old)	84	16.7
" (2 - 4 days old)	104	15.8
" (4 - 6 days old)	71	12.0
" (6 - 8 days old)	63	8.9
Nymph (1st instar) unfed, 1 day post-hatching	102	6.2
" (") 2 days after feeding	82	6.1
" (2nd instar) "	83	6.0
" (3rd instar) "	65	5.7
" (4th instar) "	56	5.8
" (5th instar) "	57	6.1
Adult (2nd day after first feeding)	61	4.2

(2) SO_2; mg/l needed for 50% and 99.9% kills of starved and fed Cimex lectularius; various life cycle stages: 1232

Stage	Concentration SO_2 To Yield (mg/l)		
	50% Kill	99.9% Kill (by extrapolation)	100% Kill
1st instar nymph (0 - 2 days after feeding)	3.81 ± .05	5.5	6.1
" (2 ")	3.66 ± .12	-	-

(2) SO_2; mg/l needed for 50% and 99.9% kills of starved and fed Cimex lectularius; various life cycle stages (Continued):

Stage	Concentration SO_2 To Yield (mg/l)		
	50% Kill	99.9% Kill (by extrapolation)	100% Kill
1st instar nymph (4 days after feeding)	3.36 ± .04	4.7	-
2nd " (14 days post moult; unfed)	4.08 ± .15	8.9	-
5th " (2 days post feeding)	4.60 ± .06	6.8	6.1
5th instar nymph (1 day post moult; unfed)	3.01 ± .12	5.8	-
" (14 days ")	5.3 ± .05	6.3	-
" (49 " ")	5.58 ± .21	12.0	-
Adult (2 days after 3rd feeding)	2.47 ± .08	3.9	-
" (28 ")	3.12 ± .18	6.8	4.2

(3) For control of Cimex lectularius 60 - 80 fluid ounces (= 90 - 120 ounces by weight) per 1000 ft³ as liquid SO_2 is recommended. 1294

g) Addendum: Recent data on toxicity of SO_2 for certain insects, derived from tests of the gas in fumigant mixtures for grain treatment: 1773

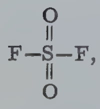
Insect And Stage	LC_{50} (mg/l) At Exposure Shown (Hrs) (At 25 C)			LC_{95} (mg/l) At Exposure Shown (Hrs) (At 25 C)		
	5 Hrs.	1 Hr.	0.5 Hr.	5 Hrs.	1 Hr.	0.5 Hr.
Attagenus piceus (larva)	11.2	16.5	25.6	16.0	23.2	35.2
Tribolium confusum (egg)	7.8	18.9	39.2	9.1	25.6	53.6
Tribolium confusum (adult)	6.8	7.8	9.8	8.0	9.9	12.2
Sitophilus granarius (adult)	5.4	11.5	12.2	6.7	13.0	13.8

(1) SO_2 is highly sorbed and/or "reacted" in grain (corn). 1773

(2) In fumigation mixtures, surface-applied, SO_2 has no appreciable penetration effect below the grain surface. 1773

170

SULFURYL FLUORIDE (Vikane [Dow Chemical Company])



$F-S(=O)_2-F$, SO_2F_2 Molecular weight 102.066

GENERAL

(N.B. The data which appear in this section derive from a recent paper, Kenaga, E. E., The Journal of Economic Entomology 50(1): 1, 1957, to which attention was drawn too late for inclusion in the alphabetic, cumulative bibliography of the present work.)

A new fumigant, introduced for use in the control of structural- and commodity-insect pests. In laboratory tests, sulfuryl fluoride has been found to possess the attributes of a good insect fumigant, being: Toxic to insects under all conditions of temperature and exposure, non-explosive, easily dispersed, essentially non-reactive, relatively non-sorptive in commodities, and having rapid penetration through insect-infested stored products. Sulfuryl fluoride is stated to be of outstanding value in the control of insects, including the drywood termite, Kalotermes minor, as reported by Stewart, D., The Journal of Economic Entomology 50(1): 7, 1957.

PHYSICAL, CHEMICAL

A gas (at ordinary temperatures), non-inflammable, colorless, odorless; b.p. -55.2°C at 760 mm Hg—a boiling point lower than any commercial insecticidal fumigant; m.p. -136.67; v.p. 13,442.0 mm at 25°C (260 lbs/in² or ca. 18 atmospheres, at -5°C having a v.p. ca. 3 times that of methyl bromide at 40°C); easily dispersed under conditions of low temperature the high v.p. also enhances gaseous penetration of commodities and structural materials; heavier than air as a gas, heavier than water as a liquid; $d_{4^\circ}^{25^\circ}$ 1.342 (as liquid), as gas 3.52 (air = 1); latent heat of vaporization at b.p. 4,600 (± 5%) calories/mole; air saturation concentration at 5°, 10°, 25°, 40°C =

> 200 lbs/1000 ft³ or complete displacement of all air without condensation at 1 atmosphere; ppm at 1 lb/1000 ft³ = 3,832; solubility:

°C	g SO_2F_2 /100 g Solvent			
	Water	Cottonseed Oil	Peanut Oil	Propylene Glycol
0	0.16	0.94	-	-
10	0.10	0.87	-	-
20	-	0.78	-	-
25	0.075	-	0.62	0.2
40	0.07	0.59	-	-

at 22°C g SO_2F_2 /100 g solvent: Acetone 1.74; chloroform 2.12; ethylene dibromide 0.5; Stoddard's solvent 0.77; isopropyl formate 1.4; propylene oxide 0.62; at -78°C soluble to infinity in methyl bromide; may be safely used on a wide assortment of common household materials with no corrosion, residual odor or color change after 16 hrs. based on exposure, at 80°F, to an atmosphere with 3 lbs SO_2F_2/1000 ft³ of the following: stainless steel, brass, copper, aluminum, zinc, silver, butyl rubber, buna rubber, buna H rubber, polyacrylon rubber, neoprene rubber, thiokol rubber, saran rubber, natural rubber, sponge rubber, cork rubber sole, neolite sole, Orlon, Nylon, Dacron, acetate Rayon, wool, cotton, wool suiting and wallpaper colors (many), cowhide (6 kinds), suede (blue), kid leather (black, white), horsehide.

Comparative physical data, SO_2F_2 and other fumigants:

Compound	B.P. (760 mm) (°C)	V.P. (mm) At				$d^{25°}_{4°}$	d (gas) (air = 1)	Latent Heat Of Vaporization (calories/M)	ppm At 1 lb/ 1000 ft³
		-5°C	10°C	25°C	40°C				
SO_2F_2	-55.2	6,255.0	9,150.0	13,442.0	19,646	1.342	3.52	4,600 ± 5%	3,832
CH_3Br	4.5	550.0	940.0	1,580.0	2,500	1.732 (0°/0°)	3.28	5,750	4,116
CS_2	46.2	98.0	195.0	361.6	620	1.256	2.62	6,399	5,147
CCl_4	76.5	24.0	54.0	114.5	210	1.584	5.31	7,140	2,543
Ethylene dichloride	83.0	17.5	41.0	79.9	164	1.246	3.41	7,652	3,913
Ethylene dibromide	131.6	2.7	6.7	11.6	30	2.17	6.48	7,688	2,071

Air saturation concentrations, SO_2F_2 and other fumigants:

Compound	Air Saturated (At 1 Atmosphere) Lbs/1000 ft³ At			
	-5°C	10°C	25°C	40°C
SO_2F_2	>200*	>200*	>200*	>200*
CH_3Br	195.5	>200*	>200*	>200*
CS_2	27.9	53.9	94.9	155.3
CCl_4	13.8	29.5	56.7	103.6
Ethylene dichloride	6.5	14.4	26.6	52.0
Ethylene dibromide	1.9	4.4	7.3	18.1

* Complete displacement of all air without condensation.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) No quantitative data are presented to indicate the toxicity of SO_2F_2 to man and other mammals or birds. Male and female rats, Guinea pigs, rabbits and female *Rhesus* monkeys tolerated 100 ppm SO_2F_2 in exposures of 7 hours per day, 5 days per week for 6 months without adverse effects on growth, general aspect, behaviour and normality of internal organs at post-mortem. While not as toxic as many commonly used fumigants, SO_2F_2 requires safe handling precautions. It is reported to be one third as toxic as methyl bromide when measured under single exposure in acute inhalation tests.
   b) Turtles, frogs (tadpoles), ram's horn snails (genus or species not given in any instance) are stated to have been killed when exposed to SO_2F_2 in 4 liters of water at a dosage of 24 oz per 1000 ft³ at 80°F, for 16 hrs in a 25.5 liter fumigation vault (similar exposure, etc. used vs. 14 species of tested insects).

2) Toxicity for insects:
   a) Toxicity of SO_2F_2 for various insect species, and life cycle stages, exposed for 16 hrs at 80°F in 25.5 liter empty fumigation vaults:

Insect	Stage	LC_{50} ± 95% Fiducial Limits (ounces/1000 ft³)*	LC_{95} ± 95% Fiducial Limits (ounces/1000 ft³) *
Tribolium confusum	Adult	3.14 ± .45	3.45 ± .46
Tribolium confusum	Egg	42.7 ± 93.4	70.3 ± 93.8
Sitophilus granarius	Adult	0.63 ± .25	0.91 ± .23
Sitophilus granarius	Pupa	0.76 ± .46	0.86 ± .46
Sitophilus granarius	Larva	0.36 ± .33	0.86 ± .33
Sitophilus granarius	Egg	24.9 ± 43	49.6 ± 44

2) a) Toxicity of SO_2F_2 for various insect species, and life cycle stages, exposed for 16 hrs at 80° F in 25.5 liter empty fumigation vaults (Continued):

Insect	Stage	LC_{50} ± 95% Fiducial Limits (ounces/1000 ft^3)*	LC_{95} ± 95% Fiducial Limits (ounces/1000 ft^3) *
Rhyzopertha dominica	Adult	0.19 ± .72	0.65 ± .65
Rhyzopertha dominica	Pupa	0.60 ± .47	1.31 ± .47
Rhyzopertha dominica	Egg	8.45 ± 6.38	13.70 ± 6.16
Oryzaephilus surinamensis	Adult	0.78 ± .31	0.87 ± .31
Attagenus piceus	Larva	2.08 ± .63	2.39 ± .63
Attagenus piceus	Egg	42.3 ± 95.3	75.8 ± 95.1
Lasioderma serricorne	Adult	0.71 ± .21	0.94 ± .24
Epilachna varivestis	Egg	17.96 ± 5.49	20.17 ± 5.72
Cynaeus angustus	Adult	1.89 ± .43	2.31 ± .44
Cynaeus angustus	Larva	2.17 ± 1.08	2.22 ± 1.07
Periplaneta americana	Adult	0.46 ± .27	0.59 ± .27
Periplaneta americana	Egg	19.41 ± 9.86	25.80 ± 9.93
Blattella germanica	Adult	0.77 ± 1	1.16 ± 1
Sitotraga cerealella	Adult	0.74 ± .45	1.32 ± .47
Sitotraga cerealella	Larva	0.82 ± .39	1.50 ± .40
Sitotraga cerealella	Egg	4.81 ± 2.85	5.44 ± 3.0
Anagasta kühniella	Adult	1.35 ± .89	2.14 ± .86
Anagasta kühniella	Larva	1.1 ± .21	2.6 ± 2.12
Prodenia eridania	Egg	18.21 ± 6.74	22.7 ± 6.89
Musca domestica	Adult	0.54 ± .33	0.96 ± 0.33
Musca domestica	Pupa	0.96 ± .41	1.36 ± .42

* Equivalent to milligrams/liter.

b) Effects of temperature and exposure time on toxicity of SO_2F_2 and CH_3Br:

Exposure (Hrs)	°F	Tribolium confusum (adult)				Attagenus piceus (larva)			
		ounces/1000 ft^3							
		SO_2F_2		CH_3Br		SO_2F_2		CH_3Br	
		LC_{50}	LC_{95}	LC_{50}	LC_{95}	LC_{50}	LC_{95}	LC_{50}	LC_{95}
16	80	3.14 ± .45	3.45 ± .46	3.29 ± .44	3.71 ± .44	2.08 ± .63	2.39 ± .63	3.60 ± .30	4.02 ± .48
16	60	3.78 ± .19	4.0 ± .19	3.87 ± .48	4.74 ± .48	2.51 ± .58	3.36 ± .56	4.21 ± 1.44	4.70 ± 1.76
16	40	6.29 ± .75	7.38 ± 1.76	9.22 ± 3.04	11.95 ± 3.2	9.68 ± 3.84	13.0 ± 3.84	11.10 ± 2.88	14.54 ± 3.04
5	80	6.86 ± 1.36	8.06 ± 1.47	8.34 ± 1.22	9.49 ± 1.71	5.19 ± 3.04	6.75 ± 3.04	8.64 ± 3.2	9.60 ± 3.36
2	80	12.77 ± 2.88	14.32 ± 4.32	20.03 ± 8.8	22.75 ± 9.12	11.71 ± 2.24	14.25 ± 2.24	18.72 ± 1.2	24.48 ± 1.25
1	80	19.36 ± 2.24	22.56 ± 2.4	29.92 ± 11.52	36.0 ± 14.4	18.4 ± 13.12	26.32 ± 13.12	29.92 ± 4.8	36.16 ± 5.76
0.5	80	36.16 ± 15.84	43.84 ± 15.84	46.08 ± 14.08	55.2 ± 14.24	27.84 ± 11.20	42.08 ± 10.72	48.58 ± 23.36	53.90 ± 23.36

c) Relative penetration properties of SO_2F_2 and CH_3Br in various goods at a dosage of 8 oz. per 1000 ft^3, 80°F, 16 hrs exposure; Attagenus piceus (larva), Tribolium confusum (adult) = test insects:

Goods	Particle Size (Average $\mu\mu$)	pH (water slurry)	Depth At Which Insects Exposed (in.)	% Mortality With			
				CH_3Br		SO_2F_2	
				Attagenus	Tribolium	Attagenus	Tribolium
"Mike" sulfur	5	7.6	1	100	100	100	100
"	5		5	98	100	100	100
"	5		9	55	100	100	100
Wheat Gluten	30	5.5	1	100	100	100	100
"	30		5	3	3	100	100
"	30		9	3	3	100	100
Hardwood Flour	10	4.9	1	82	100	100	100
"	10		5	0	15	100	100
"	10		9	0	6	100	100
Powdered Milk	10	6.7	1	100	100	100	100
"	10		5	100	100	100	100
"	10		9	100	100	100	100
Barden Clay	8	5.3	1	100	100	100	100
"	8		5	100	100	100	100
"	8		9	61	100	100	100
White Wheat Flour	25	5.4	1	100	100	100	100
"	25		5	12	85	100	100
"	25		9	3	9	100	100
Ground Tobacco	5	6.5	1	100	100	100	100
"	5		5	100	61	100	100
"	5		9	27	0	100	100

d) Relative penetration properties in various types and moistures of soil of SO_2F_2 and CH_3Br at 80°F; 16 hrs exposure to a dosage of 8 oz./1000 ft^3; * = lowest concentration tested:

Soil Type	% H_2O w/w	Depth At Which Insects Exposed (in)	Ounces/1000 ft^3 To Yield Ca. 100% Kills			
			SO_2F_2		CH_3Br	
			Attagenus	Tribolium	Attagenus	Tribolium
Sand	0	1	4*	4*	4	4
"	0	5	4*	4*	4	6
"	0	9	4*	4*	4	6
Clay Loam	0.5	1	4*	4	6	4
"	0.5	5	4*	6	8	8
"	0.5	9	4*	6	8	8
Clay Loam	7.8	1	4*	4	4*	4*
"	7.8	5	4*	6	6	4*
"	7.8	9	4*	6	6	4*
Clay Loam	15.7	1	4*	4*	4*	4*
"	15.7	5	4*	6	6	4
"	15.7	9	4	6	6	6
Peat	2.0	1	4*	4*	6	6
"	2.0	5	4*	4*	8	8
"	2.0	9	4*	4*	16	16
Peat	47.5	1	6*	6*	6*	6*
"	47.5	5	6*	6*	6*	6*
"	47.5	9	6*	6*	6*	6*

e) Comparative sorption in whole grain wheat of SO_2F_2 and CH_3Br:
   (1) Test conditions deliberately exaggerated: 48°F, 14 day exposures, dosages 96, 64, 32 oz/1000 ft^3; 30 lbs wheat (moisture content 13 - 14.5%) in 25.5 liter fumigation vaults with ca. 50% air space load; fumigants introduced as vapor under vacuum with vault then brought to atmospheric pressure and rolled for quick gas distribution through the wheat.
   (2) Results: Depending on concentration and length of exposure, SO_2F_2 was sorbed to the extent of 14 - 43% of the amount of CH_3Br sorbed under the same circumstances.

3) Pytotoxicity:

a) In germination tests of various seeds, Oryza sativa (13.6% moisture), Triticum aestivum (12.6% moisture), Avena sativa (15.7% moisture), Secale cereale, Zea mays (12.3% moisture), Sorghum vulgare (12.5 - 14.5% moisture), Linum usitatissimum, Panicum mileaceum, Phaseolus vulgaris (16 - 18% H_2O), Phaseolus limensis, Vicia faba, Vigna sinensis, Beta vulgaris, Brassica rapa, Allium cepa, Cucurbita sativa, Raphanus sativus, Medicago sativa, Euphorbia esula, Asclepias syriacus, Rumex acetosella, Amaranthus retroflexus, Melilotus sp., Trifolium pratensis, Ambrosia artemisiifolia, Sorghum halepense, Digitaria sanguinalis, Bromus inermis, Agropyron repens, were subjected to 16 hrs exposure at 80°F to 80, 40, 16 ounces of SO_2F_2 per 1000 ft^3 and then tested in sprouting tests. All treated seeds germinated just as well as the controls.

b) SO_2F_2 vs. fresh fruits, vegetables, tubers, and growing plants:
   (1) At concentrations normal in structural fumigation, for instance 1 lb per 1000 ft^3, SO_2F_2 injured severely or killed Bougainvillea, Eugenia, Nasturtium, Poinsettia, Pyracantha, Valencia orange seedlings, Veronica and ivy.
   (2) Effects of SO_2F_2 on plant material exposed 2 hrs at 80°F:

Ounces/1000 ft^3	Plant	Stage	Effect
48	Apple	Fruit	Browns skin, flesh; decay enhanced.
16	Apple	Fruit	Browns skin, flesh; half rotten in 10 days.
48	Orange	Fruit	Browns skin, desiccates, decay speeded.
16	Orange	Fruit	Color unharmed, desiccated 10% of skin.
48	Potato	Tuber	Slight "russetting."
16	Potato	Tuber	Very slight "russetting."
48	Celery	Stalk	Spotted, brown, rapidly desiccated.
16	Celery	Stalk	Spotted, brown, rapidly desiccated.
48	Tomato	Fruit	Skin spotted, brown, quick spoilage.
16	Tomato	Fruit	Unspotted, quick spoilage.
48	Tomato	Plant	Dead in a few days.
16	Tomato	Plant	Dead in a few days.
48	Corn	Plant	Dead, save for roots, in a few days.
16	Corn	Plant	Dead, save for roots, in a few days.

4) Miscellaneous:

a) Comparative penetrability of SO_2F_2 and CH_3Br through sawdust, using Kalotermes minor as test organism; termites exposed under 44 grams of air-dry, mill-run sawdust, tamped into a column 28 cm. in height over the insect chamber at 21°C for 24 hrs:

4) a) Comparative penetrability of SO_2F_2 and CH_3Br through sawdust, using Kalotermes minor as test organism (Continued):

Compound	mg/liter	Mortality (%) 5 Days After Exposure Of Kalotermes minor
SO_2F_2	2.2	94
CH_3Br	2.4	7

(1) SO_2F_2 and CH_3Br in *in vitro* tests proved approximately equitoxic toward Kalotermes minor, however, the development of toxic signs is slower in case of CH_3Br, and it is not until ca. 24 hrs after exposure that the toxicity of CH_3Br and SO_2F_2 appears approximately equal at the LD_{96} - LD_{100} dosage level. Termites not dead after 3 - 5 days post-exposure lived on for several weeks or longer.

171

SYNERGISTS; SYNERGISM (Also consult Pyrethrins, Allethrin, Cyclethrin)

GENERAL REMARKS [Refs.: 353, 1221, 851, 2231, 1755, 1597, 3037, 263, 2515, 3258, 3008, 1347, 2575, 253, 508, 699, 3380, 2344, 3139, 2432, 249, 1560, 2012, 1779, 324, 2590, 1508, 1510, 2146, 916, 1160, 1344, 2782]

In pharmacology the term synergism has been applied when two drugs (each physiologically active of itself) jointly given to an organism, yield a combined response greater than the sum of the independent effect of each drug at the dosage administered.

The type of synergism with which this section is concerned, if it can properly be called synergism at all, in the strict sense, constitutes a special case. The term is retained because it has been loosely and generally used in the insecticide field. Strictly viewed, the subject matter here concerns, rather, activation and/or potentiation.

Much interest has grown out of the observation that the toxic effect, or kill of insects, to be had from a given amount of pyrethrins (or pyrethrin-like substances, such as allethrin) is sharply increased when the pyrethrin is applied in combination with various substances relatively non-toxic in themselves. This observation, essentially, defines the sense in which synergism and synergist is here used, namely, activation or potentiation by a substance, given at a dosage at which it is non-toxic or independently ineffective, of a toxic agent to yield an effect decidedly greater than that to be expected when the given amount of toxicant is administered alone. The object of combining with an insecticide a non-toxic "synergist" is to increase the mortality yielded by a given quantity of insecticide. This last may be viewed as a sparing action—the synergist greatly decreases the amount of toxicant which must be used to yield a given mortality of insects.

Such an effect was first noted (using a synthetic synergist) by combining pyrethrum with isobutyl undecyleneamide. Since the most clearcut examples of synergistic action of non-toxic substances with insecticides occur in the combined action of pyrethrins, allethrin, and certain other pyrethrin-like compounds with synergists the present discussion confines itself, really, to pyrethrin synergists. Furthermore, most of the insecticide synergists presently known are effective only with pyrethrins. However, observations of synergism are not confined to pyrethrins. Synergism of DDT with a long list of halogenated hydrocarbons has been claimed. Rotenone and Ryania action enhancement by some pyrethrin synergists and other substances has been reported. Certain indanediones, for instance Valone®, are reported synergistic with pyrethrins and lindane. Synergism between certain organic phosphorus insecticides and various compounds has been reported.

INSECTICIDE SYNERGISTS, ACTIVATORS, INTENSIFIERS

1) Certain organic compounds can replace part of the pyrethrins in pyrethrum insecticide formulations without reducing paralytic or insecticidal power. An increased effectiveness in some cases results from the combination. However, these substances are not necessarily limited to an effectiveness in combination with pyrethrins only, nor are they all equally useful with pyrethrum, or non-toxic for warm-blooded animals. 3037

2) Among the more prominent of pyrethrum synergists are:
   (1) N-isobutyl undecyleneamide, q.v.
   (2) sesamin, q.v.
   (3) piperonyl cyclonene, q.v.
   (4) piperonyl butoxide, q.v.
   (5) n-octyl sulfoxide of isosafrole (Sulfoxide®), q.v.

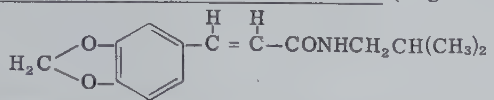
(6) n-propyl isome, q.v.
(7) N-(2-ethylhexyl)-bicyclo- [2,2,1] -5-heptene-2,3-dicarboximide, q.v.

a) N-isobutyl undecyleneamide and related substances:

(1) N-isobutyl undecyleneamide, $CH_2=C(CH_2)_8CONHCH_2CH(CH_3)_2$, used alone vs. Musca domestica is of 3258
no value; 40 mg pyrethrins + 420 mg N-isobutyl-undecyleneamide per 100 cc kerosene is more effective than a standard spray containing 100 mg pyrethrins per 100 cc. A distinct and characteristic histopathological action in insects is claimed for this synergist and pyrethrins.

(2) Relatives of N-isobutyl undecyleneamide (most being of natural [plant] origin) which either synergize with pyrethrins, or are themselves insecticidal, in some instances more so than pyrethrum, are listed below. Most of these substances are also isobutylamides of unsaturated aliphatic acids.

(a) N-isobutyl-3,4-methylenedioxicinnamide (Fagaramide): 1224,3084,1166



; with pyrethrins in the ratio fagaramide 4: pyrethrins 1. 2 mg: 0.5 mg are reported to kill Musca as effectively as a solution of twice as much pyrethrin content.

(b) N-isobutyl-4,6-decadieneamide (Spilanthol), $CH_3(CH_2)_2CH=CHCH=CH(CH_2)_2CONHCH_2CH(CH_3)_2$ 1140
is reported to be an effective mosquito larvicide. 122,1211

(c) N-isobutyl-2,6-decadieneamide (Pellitorine), $CH_3(CH_2)_2CH=CH(CH_2)_2CH=CHCONHCH_2CH(CH_3)_2$, 2468
toxicity for Musca reported as somewhat more than ½ that of pyrethrins. 2469,1668,1291

(d) N-isobutyl-2,6,8-decatrieneamide, $CH_3CH=CHCH=CH(CH_2)_2CH=CHCONHCH_2CH(CH_3)_2$, reported 1672
to be more toxic for Musca than pyrethrins.

(e) N-isobutyl-2,8-dodecadieneamide (Herculin), $CH_3(CH_2)_2CH=CH(CH_2)_4CH=CHCONHCH_2CH(CH_3)_2$, 1667
reported to be about equal to pyrethrins in toxicity for Musca.

(f) N-isobutyl-2,4,8,10,14- (or 2,4,8,12,14-) octadecapentaenamide, $CH_3(CH_2)_2CH=CH(CH_2)_2CH=$ 1670
$CHCH=CH(CH_2)_2CH=CHCH=CHCONHCH_2CH(CH_3)_2$ or $CH_3(CH_2)_2CH=CHCH=CH(CH_2)_2CH=$
$CH(CH_2)_2HC=CHCH=CHCONHCH_2CH(CH_3)_2$, (Scabrin) reported to be appreciably more toxic than
pyrethrins for Musca.

The above naturally occurring substances showed the rapid paralytic "knockdown" of insects char- 655
acteristic of pyrethrins. Saturation of double bonds yielded loss of all insecticidal action, although 1669
N-isobutyllauramide (saturated herculin) showed some synergism with pyrethrins. Cis-trans- and
trans-trans- isomers of pellitorine were non-toxic for Musca.

(g) N-isobutyl-2,4-decadieneamide, $CH_3(CH_2)_4CH=CHCH=CHCONHCH_2CH(CH_3)_2$ and N-isobutyl-2-dodeceneamide, $CH_3(CH_2)_8CH=CHCONHCH_2CH(CH_3)_2$, when synthesized, were found to yield rapid paralysis ("knockdown"), but very low kills of Musca.

b) Piperonyl or methylene dioxyphenyl derivatives:

(1) Unlike any other oil of vegetable or piscine provenance, sesame oil (from the seeds of Sesamum 3037
indicum) while non-toxic of itself, markedly enhances the effectiveness of pyrethrins for Musca killing. 891
The effect is that of a true activator, or synergist, intensifying the killing power of the toxicant, for 888,889
example:

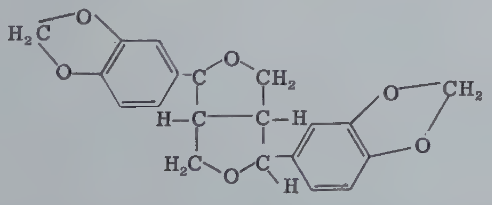
(a) Musca treated with pyrethrins alone: 100% torpid in 0.25 hr recovered to 92% in 3 hrs; addition of 1%, 3%, 5% sesame oil reduced the recovery respectively to 77%, 60%, 12%.

(b) Musca still torpid 6 hrs. after pyrethrin treatment rarely if ever recovers.

(2) Activity resides principally in certain fractions of sesame oil, for example: 461,1347,376,563

(a) Pyrethrins at 1 mg/cc in kerosene yielded 99% KD of Musca in 10 minutes with 21% kill in 24 hrs; 1428
the same amount of pyrethrin + 10 mg/cc of each of 4 sesame oil fractions yielded throughout, 2231
100% KD in 10 minutes and 24 hr kill as follows: fraction I 100%, II 91%, III 21%, IV 29%. 1350

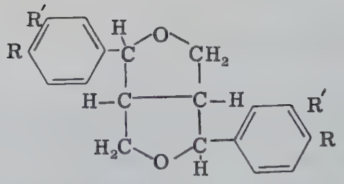
(b) From the 2 most active fractions may be isolated a crystalline solid sesamin:



a bicyclodihydrofuran symmetrically substituted with 2 methylenedioxyphenyl groups; 4 assymetric carbons, natural product dextro-rotatory which, at 2.5 mg/cc, yielded no 10 minute KD and but 5% kill in 24 hrs of Musca; pyrethrins, which at 1 mg/cc yielded 100% 10 minute KD and 20% 24 hrs kill of Musca, combined with sesamin (2.5 mg/cc) yielded 100% 10 min. KD and 85% 24 hrs. kill. A non-crystalline residue combined with pyrethrin 2.5 mg:1 mg/cc yielded 100% 10 min. KD, and 89% 24 hrs kill of Musca. No other crystalline material than sesamin could be obtained from the initial active fractions of sesamum oil.

(c) Pyrethrins and sesamin are each reported to yield a distinct histopathological effect in insects. When the agents act in combination these effects are summated.

(d) Various plants yield compounds related to sesamin, for instance, asarinin, pinoresinol and eudesamin, related to sesamin as follows:


R'
R
H
O
CH₂
H–C
C–H
R'
R
H₂C
O
C
H

where R,R' = O_2CH_2 (methylene dioxy):
Sesamin, asarinin;
R = OH, R' = OCH_3: Pinoresinol
R,R' = OCH_3: Eudesamin.
Asarinin is laevo-rotatory and thus, the optical antipode of isosesamin.

(e) Isosesamin, asarinin are as effective as sesamin in pyrethrin activation.

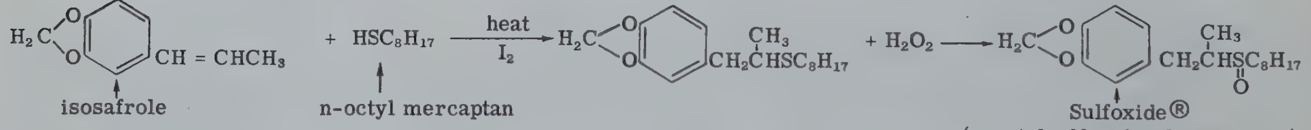
(f) Pinoresinol dimethyl ether, pinoresinol, pinoresinol diacetyl derivative yield no synergistic or activating action on pyrethrins vs. *Musca*.

(3) Importance of the methylene dioxyphenyl grouping for pyrethrin synergism; sesamin and related compounds: 2782

Substance	Concentration (%)	Average Mortality 24 Hrs, *Musca*, (%)
Sesamin	0.2	4
" + pyrethrins	.2 + .05	84
Isosesamin	.2	5
" + pyrethrins	.2 + .05	87
Asarinin	.2	14
" + pyrethrins	.2 + .05	88
Pyrethrins	.05	25
Pinoresinol	.18	1
" + pyrethrins	.18 + .05	12
Dimethyl pinoresinol	.2	1
" + pyrethrins	.2 + .05	17
Diacetyl pinoresinol	.03	2
" + pyrethrins	.03 + .05	2
Pyrethrins	.05	19

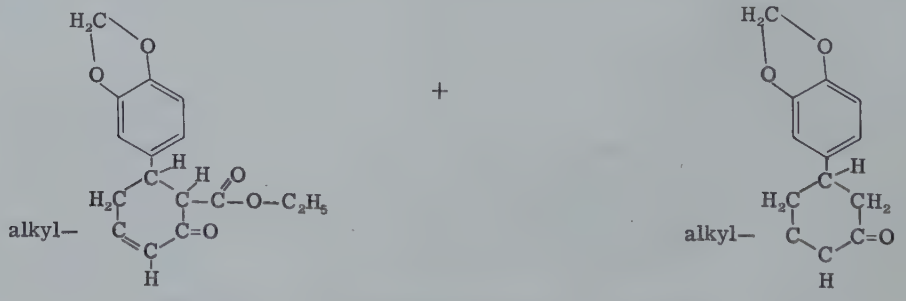
(a) Synergistic action is shown only, to any interesting extent, by the materials with a methylene 2542,2544
dioxy grouping at R, R'. 3041,3040

(b) Various synthetics with this grouping have been prepared and reported (notably, derivatives of 2546,1154
safrole) by the addition of various aldehydes, mercaptans, maleic acid esters and other com- 1421,1444
pounds to the double bond of safrole and isosafrole, for example: 3039,1476,3209,2151,2782

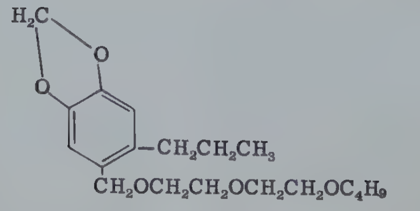

H₂C
O
O
CH = CHCH₃
isosafrole
+ HSC₈H₁₇
n-octyl mercaptan
heat
I₂
H₂C
CH₃
CH₂CHSC₈H₁₇
+ H₂O₂
H₂C
CH₃
CH₂CHSC₈H₁₇
O

Sulfoxide®
(n-octylsulfoxide of isosafrole)

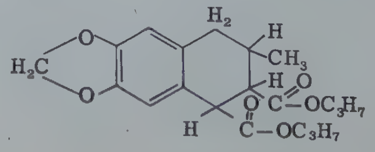
Others are derivatives of piperonal, piperonylic acid, piperine and related compounds. These studies have yielded the commercially exploited synergists piperonyl cyclonene, piperonyl butoxide and n-propyl isome, diverse substances all characterized by the methylenedioxy phenyl-grouping as shown below:


H₂C
O
O
H
C
H
O
H₂C
C–C–O–C₂H₅
alkyl–
C
C=O
C
H
+
H₂C
O
O
C
H
H₂C
CH₂
alkyl–
C
C=O
C
H

80% ⟶ piperonyl cyclonene ⟵ 20%


H₂C
O
O
–CH₂CH₂CH₃
CH₂OCH₂CH₂OCH₂CH₂OC₄H₉

piperonyl butoxide


H₂
H
CH₃
H
O
H₂C
O
O
C–OC₃H₇
O
H
C–OC₃H₇

n-propyl isome

c) Toxicity of certain commonly used synergists for mammals: [Refs.: 1951, 1952, 831, 1953, 2951]

Compound	LD_{50} (mg/k) For	
	Rat (Oral)	Rabbit (Cutaneous)
Piperonyl butoxide	7500 - 12,800	1880
Piperonyl cyclonene	ca. 5200	Multiple daily 100 mg/k doses tolerated
n-Octyl sulfoxide of isosafrole	ca. 2000	> 9000
n-Propyl isome	ca. 15,000	> 375
N-(2-Ethylhexyl)-bicyclo [2,2,1] -5-heptene-2,3-dicarboximide	2800	470

(1) Sesamin, Sesame oil are non-toxic; sesame oil and sesame seed are extensively used food items.

d) Mode of action of insecticide synergists:

(1) Certain factors which have been variously proposed to account in whole or in part for the action of synergists: Increase in the dose of poison received by insects in flight through insecticidal mists by stabilization of droplet size; by stimulating flight activity; other proposed actions are: Reduction in "knockdown" rate, prevention of toxicant deterioration and increasing the effectiveness of the doses of toxicant applied to or received by the insect. The last proposal, of course, explains nothing, since it merely states what the synergist operationally is known to do. These proposals have been dealt with succinctly in the reference given, and will not be summarized here. 2231

(2) Some workers have demonstrated to their satisfaction that in the case of sesamin and isobutyl undecyleneamide the synergistic effect remains when all physical factors (droplet size, stabilization, etc.) which have been brought forward are taken account of and eliminated as factors. 2432,2431 249

(a) Dismissing the histopathological effects observed by some, these workers declare these effects to be out of the practical synergistic effect range and reproducible by simple anaeroxia.

(b) Proposing that pyrethrin acts on the insect peripheral nerve system at a site a few micra from the external surface they suggest a surface complex between synergist-toxicant at the peripheral nerve sheath interfaces which so orientates the pyrethrin molecule that it produces a more efficient discharge of nerve resting potential at the interface.

(c) Increase of pyrethrin toxicity by a factor of 3, when up to equimolecular proportions of the above synergists was added, was noted; further additions of synergist gave no increased effect. Addition of synergist decreased the mean weight of pyrethrins needed to paralyze a single *Aëdes aegypti* adult from 6.0 to 2.0 times 10^{-7} mg but once a 1:1 molecular ratio was achieved no further decrease of KD threshold-weight of pyrethrins was possible. Vs. *Sitophilus granarius* the increase in toxicity of pyrethrins to a 3 fold degree at equimolar proportions and no further increase with greater proportions of synergist, was also attested.

(d) In further studies using N-isobutyl undecyleneamide, sesamin, ethylene glycol ether of pinene, piperonyl butoxide, piperonyl cyclonene, n-propyl isome and N-(2-ethyl hexyl)-bicyclo- [2,2,1] -5-heptene-2,3-dicarboximide a sharp limitation of increase in synergistic action at equimolecular proportions of pyrethrin and synergist was confirmed for flying *Aëdes* and for *Sitophilus* crawling upon synergized pyrethrin deposits. Only in case of piperonyl butoxide was the equimolecular limiting relative potency not attained.

(3) The foregoing conclusions are disputed by those who assert that increased potentiation of toxicant continues to a 10:1 molar ratio of synergist to pyrethrin, and who find no evidence for a complex of synergist-pyrethrin in the instance of piperonyl butoxide. 1154 2266

(a) Others, using the measured drop method to test N-isobutyl undecyleneamide and piperonyl butoxide as pyrethrin and allethrin synergists vs. *Musca domestica* and *Cimex lectularius*, noted increase in pyrethrin toxicity with a rise in the ratio of synergist to toxicant to at least 20:1. Enhancement was greatest in the range of lower ratios. Piperonyl butoxide was found the most potent synergist, increasing pyrethrin potency 5 times and allethrin potency 4 times vs. *Musca*, pyrethrins 2 times and allethrin 3 times vs. *Cimex*. Piperonyl butoxide greatly prolonged the time of effectiveness of pyrethrin films (residual effect). N-Isobutyl undecyleneamide did not enhance pyrethrin potency by more than 2 times for either test insect. It is to be kept in mind that pyrethrins are twice as toxic as allethrin for *Musca* and 5.5 times as toxic for *Cimex*. 2344

(4) Pretreatment of *Musca* with a synergist brought a result (with subsequent application of pyrethrins in sub-lethal dose) in no way different than if synergist + pyrethrin had been applied at the same time; the reverse, however, failed to yield synergism. 2012

(5) Synergist and toxicant may be applied to widely different areas of the insect body (*Musca*) without loss of synergistic action; this is deemed to rule out any enhancement of penetration on the part of the toxicant by the synergist. 3318 508 699

(6) Some studies suggest that the synergist extinguishes the general resistance shown by *Musca* to pyrethrins at high temperature as opposed to low (negative temperature coefficient in respect to toxic effect). It was postulated that a detoxification mechanism, active at higher temperatures to protect the insect from pyrethrin, is blocked by the synergist at those temperatures at which the detoxification is normally most active. 508,3380 3333 3397

(7) N-Isobutyl undecyleneamide synergizes with pyrethrins in louse powders vs. *Pediculus humanus corporis* apart from considerations of droplet size, residue protection, etc., rendering pyrethrins 100 times as efficient in killing power when compared with the same amount of pyrethrin used without the synergist (which, at the level used, was non-toxic for *Pediculus* when applied alone). Here the evidence points to some biochemical or physiological potentiation of pyrethrin. 1344

e) Histopathological Considerations:

(1) Cell and tissue changes which have been attributed to action of pyrethrins and synergists applied alone to Musca are as follows:

(a) Pyrethrins: Pycnosis of nuclear chromatin, vacuolar degeneration of neurons of the large type, 1426
nerve fiber tract degeneration. 1422

(b) N-Isobutyl undecyleneamide: Disappearance of nuclear chromatin. 1426,1422

(c) DHS Activator (ethylene glycol ether of pinene): Cytoplasmic changes in nerve tissue which accentuated prominence of fibers, an effect produced following piperine treatment also. 1422

(d) Sesamin: Vacuolar degeneration of cytoplasm in large neurons. 1422

(2) Combinations of pyrethrins with each of various synergists yielded effects characteristic of both com- 1426,
ponents used alone. 1422

(3) Changes in muscle tissue of Musca were also noted, namely: Nuclear pycnosis, disappearance of the nuclear membrane, increased prominence of such components as the membrane of Krause and nodal elements. Effects of pyrethrin differed from effects of activators; combinations yielded summation of effects.

(4) Detailed evaluations of neuropathology after treatment with pyrethrins and with Valone® (2-isovaleryl-1,3-indanedione) and 2-pivalyl-1,3-indanedione which are said to synergize with pyrethrins have been reported. See the individual treatments of these compounds. 2600

(5) The cytopathological and histopathological effects observed in moribund test insects have been discounted by some as generalized changes attending oncoming death and reproducible with anoxia alone. Others declare them to be secondary to (and symptomatic of) deeper causes due to disruption of biochemical systems by toxicant and/or synergist. 2596

f) Other considerations:

(1) Synergistic action involving nicotine and pyrethrins, given by injection to Oncopeltus fasciatus, has 3141
been reported. The two substances applied alone, or in combination (by dipping) to Tribolium confusum 3139
were not deemed synergistic but said to show "independent joint action."

g) Evidence of combined action and/or antagonism between organic phosphorus insecticides and various substances, among them known pyrethrin synergists is presented in the general treatment titled Organic Phosphates and in the section devoted to Malathion.

h) Synergists and DDT:

(1) Addition of piperonyl cyclonene, q.v., DMC, q.v., to DDT formulations tested upon various biotypes of 2476
DDT-R Musca domestica and of piperonyl butoxide to a lindane formulation tested on Tribolium cas- 2475
taneum, brought about a marked reduction in the amount of toxicant (measured as LD_{50}) required for 1225
toxic effect upon the test organisms. Sharp increases in the slopes of the dose-mortality graphs were 2091
remarked. Various other pyrethrin synergists had little if any effect in making DDT again an effective 3011
toxicant for DDT-R biotypes of Musca. Nor did the susceptibility of DDT-R biotypes return, in presence of piperonyl cyclonene, to the level of the original, unselected, parent colonies or "populations."

(2) Adding piperonyl cyclonene to DDT in tests on DDT-non R Musca biotypes did not potentiate DDT 2476
action. Indeed, in large amounts the synergist affected unfavorably the toxicity of DDT, lowering it 1078
and decreasing the slope of the graph line.

(3) Piperonyl cyclonene and DMC inhibited strongly the enzymatic system which in DDT-R biotypes of Musca rapidly detoxifies DDT by dechlorination to DDE (2,2-bis-(p-chlorophenyl) 1,1-dichloroethylene). By inhibition of this detoxifying system DDT-R biotypes behaved toward DDT much like the ordinary susceptible "populations."

(a) The ratio of piperonyl cyclonene: DDT required to yield the above effect varied from 30:1 to 100:1 (an exceedingly high ratio compared with that needed to potentiate pyrethrins at the maximum), and the magnitude of the ratio was reported to follow the degree of resistance of a particular biotype of Musca.

(4) A number of compounds (in addition to DMC) which are structural relatives of DDT have been found to 3009
potentiate the action of DDT vs. DDT-R Musca biotypes. 3008,2936,2091

(a) None of these materials, however, could restore the full effectiveness of DDT toward DDT-R Musca by reducing the amount required for LD_{50} to the level noted in the original strains of heterogeneous susceptible "populations" or colonies. Indeed, there is evidence that DDT-synergist combinations reduced the effectiveness of DDT to DDT-non-R Musca.

(b) Applications of DDT and synergist, separated in time by as much as 12 - 24 hrs., did not dampen 2091
the potentiating effect of some compounds, at least. 2473

(c) To explain the action of DMC (1,1-bis-(p-chlorophenyl) ethanol) competition with DDT for the de- 2936
hydrochlorinase which detoxifies DDT has been suggested. Structurally the synergist can form 2091
with the enzyme an enzyme-substrate complex, thus removing the detoxifying enzyme from the 2473
biochemical flux.

(d) In this connection, it may be recalled that inhibition of a pyrethrin-detoxifying system on the part of pyrethrin synergists has been proposed in explanation of the mode of pyrethrin synergist action. 3318

ADDENDUM; SOME RECENT DATA ON SYNERGISTIC COMPOUNDS AND THEIR ACTIVITIES:

1) Inhibition of development in Musca domestica by piperonyl butoxide and other 3,4-methylene dioxy phenyl compounds: 2284

a) Some 3,4-methylene dioxy phenyl-compounds, formerly deemed to be of synergistic value only, have proved toxic per se to Musca domestica when added to the larval rearing medium.

(1) These compounds brought developmental inhibition at very low concentrations. For example, the LC_{50} of isosafrole was 0.0235%.

(2) DDT-R biotypes of Musca proved as readily susceptible to the action of 3,4-methylene dioxyphenyl-compounds as did DDT-non-R biotypes.

(3) Many inhibitors of development among the tested compounds proved to be good synergists of pyrethrins, but this was not generally true.

b) Studies were made by incorporating the test substances in the CSMA (Chemical Specialties Manufacturers Association) rearing medium. Musca domestica biotypes were: Orlando-Beltsville (DDT-R) and NAIDM (National Association of Insecticide and Disinfectant Manufacturers) (DDT-non-R).

c) Tabular evidence of the behavior of tested compounds toward DDT-non-R and DDT-R biotypes of Musca domestica:

(1) N.B. R in the list of test substances signifies the 3,4-methylene dioxyphenyl-group.

Compound and Concentration In Rearing Medium	DDT-Non-R Biotype Musca		DDT-R Biotype Musca	
	Pupation Delay	Emergence (%)	Pupation Delay	Emergence (%)
At 0.125% Concentration				
1-R-1-butanol	--	--	Complete Inhibition	
4-R-3-butene-2-one	1 day	61%	2.5 days	41%
N,N-Dibutyl piperonyl amine	1 day	0	3 days	40
Isosafrole	--	--	Complete Inhibition	
3,4-Methylene dioxybenzyl analog Allethrin	1 day	9	2.5 days	41
1-R-4-phenyl-1-butanol	1 day	0	3 days	0
Piperonylic acid	1 day	--	--	--
Sesamol	3 days	--	--	--
Sulfone	--	--	Complete Inhibition	
At 0.0625% Concentration				
1-R-1-butanol	Complete Inhibition		Complete Inhibition	
2-Butoxyethyl R-acetal acetaldehyde	4 days	25	--	--
Butyl-R-acetal acetaldehyde	--	45	--	--
5-Butyl-5-ethyl-2-R-m-dioxane	Complete Inhibition		--	--
Dihydrosafrole	Complete Inhibition		--	--
Isosafrole	Complete Inhibition		Complete Inhibition	
2-Methoxyethyl-R-acetal acetaldehyde	--	54	--	--
R-ester of Butylcarbamic acid	--	45	--	--
Piperonyl alcohol	--	31	--	--
Sulfone	Complete Inhibition		Complete Inhibition	
At 0.0313% Concentration				
Dihydrosafrole	--	--	2 days	52
2-Ethylhexyl-R-ether	1 day	--	--	--
Sesamol	--	--	2.5 days	--
Sulfoxide	2.5 days	0	3 days	--

172

SYSTEMIC INSECTICIDES

GENERAL REMARKS [Refs.: 2479, 3018, 3310, 3356, 1557, 293, 2057, 719, 3256, 284, 2314, 1539, 3177, 3326, 800, 1098, 975, 2035, 2920, 1900, 182, 3134, 3135, 3093, 2651, 1695, 3257, 220, 3072, 2942, 1130, 548, 353, 2231, 2769, 703, 1625, 2355, 1405, 695, 1623, 2772, 698, 2654, 1418, 1469, 1470, 1108, 878, 1340, 1987, 1414, 3149, 1168]

There is at the present much interest in what have come to be called (although ambiguously) "systemic" insecticides. The interest has been spurred by the fact that in the general group of organic phosphorus insecticides, toxicants presently commanding much attention, there is a number of compounds with a decided and practically useful systemic action.

Systemic insecticides are those toxicants which may be absorbed by plants (by way of roots, leaves, stems, branches, trunks) and translocated generally throughout the treated plant (by way of the tissues or the sap stream) in amounts sufficient to kill insects or mites feeding on the tissues and/or juices. In addition, some systemic insecticides, after being taken up by the plant, may be themselves, or in the form of metabolites or transformation products, transpired by the plant in concentrations sufficient to exert a fumigant killing action on insects in contact with the transpiring parts. This last action may combine with the more commonly understood systemic action. Systemic action does not by any means preclude other routes of toxicity for such compounds in the ordinary sense of insecticidal action—by contact toxicity, ingestion, residual action, etc.

Systemic insecticides have long been recognized as desirable and have been long sought. The first practically useful toxicants of this general class have been certain compounds of selenium, chiefly selenites and selenates of sodium and potassium. The selenium compounds, when applied to the soil in solution or added to hydroponic media, enter the plant and exert a systemic insecticidal action which has been taken advantage of practically to protect various greenhouse crops, notably roses, chrysanthemums, snapdragons, carnations and violets from aphids, mealy-bugs and acarines. Nor have experiments on the systemic action of toxicants been limited to plants. Several researches have been undertaken with the object of using a toxicant such as valeryl indanedione or certain halogenated hydrocarbons to render the blood of higher animals toxic to biting and sucking insects and acarines.

The selenates and selenites, which have been the original toxicants purposefully employed for systemic action, also illustrate problems which are generally of concern for toxicants of this kind. Selenium compounds are toxic and hazardous for animals and for plants also. By accumulation in soil they rapidly render it unfit for many plants. For example may be cited the fact that greenhouse carnations are limited to two years of selenium treatment, after which plants and soil must be replaced. The margin of insecticidal concentrations of selenium in the plant juices and phytotoxic levels is narrow.

The foregoing disadvantages of systemic selenium toxicants place in focus certain desiderata which must be met in whole or part by any systemic insecticide. Among other things, such compounds should be able to act in low concentration, i.e. be very toxic to insects, yet be relatively without hazard for consumers of treated vegetation or its useful products. Since such substances by being as a rule highly toxic for insects are thus almost certainly toxic to higher forms, the residue hazard must be low either by degradative or detoxifying plant action or by comparatively short life. Yet these properties must be such as not to preclude effective action against insects.

Even systemic insecticides deemed too hazardous for general use may have invaluable specialized uses under conditions in which the hazard is conveniently controlled. For example, bis-(dimethylamino) fluorophosphine oxide is an effective systemic insecticide but toxic and hazardous to an intense degree for higher forms as well as for insects. None-the-less, safe means of applying BFPO to cacao trees have been worked out, and have been of great promise in protecting this plant from a serious mealy-bug pest whose habits render it almost impossible to control by conventional means. The fruit of BFPO-treated cacao trees does not, after the normal processing, retain harmful residue.

It may be expected that the field of systemic insecticides will be explored yet more intensively. In addition to the selenium compounds already mentioned, effective or promising systemic insecticides have been found among the organic phosphorus toxicants and the insecticides derived from carbamic acid. A number of these substances are listed immediately below, and their properties may be considered in detail in those sections specifically devoted to the individual listed compounds:

Diethyl 2-chlorovinyl phosphate
0,0-Dimethyl 0-1-carbomethoxy-1-propen-2-yl phosphate
5,5-Dimethyl dihydroresorcinol dimethyl carbamate, (Dimetan)
0,0-Diethyl 0-2-ethylmercaptoethyl thionophosphate, (Systox®)
0,0-Dimethyl 0-2-ethylmercaptoethyl thionophosphate, (Meta-Systox®)
3-Methyl-1-phenyl-pyrazolyl-(5)-dimethyl carbamate, (Pyrolan)
3-Methylpyrazolyl-(5)-diethyl phosphate (Pyrazoxon)
Bis-(monoisopropylamino) fluorophosphine oxide (Isopestox®)

Octamethyl pyrophosphoramide (OMPA, Schradan)
Bis-(dimethylamino) fluorophosphine oxide (BFPO)
Sodium fluoroacetate (Compound 1080)
1-Isopropyl-3-methylpyrazolyl-(5)-dimethyl carbamate (Isolan)
2-n-Propyl-4-methylpyrimidyl-(6)-dimethyl carbamate (Pyramat)
0,0-Diethyl 0-p-nitrophenyl phosphate (Para-oxon)
0,0-Diethyl S-2-isopropylmercaptomethyl dithiophosphate (TM 12008)
0,0-Diethyl S-propylmercaptomethyl dithiophosphate (TM 12009)
0,0-Diisopropyl S-isopropylmercaptomethyl dithiophosphate (TM 12013)
Diethyl bis-(dimethylamino) pyrophosphate (sym. & unsym.)
0,0-Dimethyl S-(2-oxoureidoethyl) dithiophosphate

In general, systemic activity has been directly related among organic phosphorus toxicants to solubility in water. For example, OMPA is water-miscible and systemic, Para-oxon (soluble to 0.24%) is systemic while the closely related parathion (soluble only to 0.0024%) is non-systemic, the thiolisomer of Systox® is systemic and soluble to 0.2%, while the thionoisomer, which is weakly systemic, is soluble only to 0.005 - 0.02%. However, among the organic phosphorus compounds are many which penetrate plant tissue and are sufficiently stable and soluble in aqueous media to make them promising candidates as "systemics."

TERMINOLOGY

1) Classification of systemic insecticides, in a general way, has been made according to their fate within the plant. 2651
    a) Stable systemic insecticides: Compounds which (e.g. selenates) remain unchanged chemically during their whole presence in the plant.
    b) Endolytic systemic insecticides: Compounds which after absorption and translocation are present in the plant largely in the original form, are insecticidal in that form, and continue their action in that original form, until decomposed or degraded by the plant to a concentration below the toxic level, for instance paraoxon, pyrazoxon and diethyl-2-chlorovinyl phosphate.
    c) Endometatoxic systemic insecticides: Compounds which after being absorbed and translocated (and before being ultimately degraded and detoxified) are intermediately transformed, partly or wholly, into secondary toxic substances which act insecticidally and may be more potent toxicants than the original compound, for example Systox®, Meta-Systox® and OMPA.
        (1) Of the substances showing systemic action not all, at present, can be placed in one or the other of the proposed categories.

SOME ADVANTAGES OF SYSTEMIC INSECTICIDES 2651

1) Possibility of action vs. cryptic or protected insects, for instance on plants with highly curled or crinkled leaves, cauliflower, etc.; vs. insects with protective coatings or secretions such as mealy-bugs, spittle-bugs; vs. insects feeding at the roots and not reached by conventional methods.

2) Protection of the toxicant from the vagaries of weather and deleterious influences such as light, oxygen, etc.

3) Specificity for insects harmful to plants, yet sparing of useful predators, pollinators and parasites of pest insects. For example, OMPA, while virtually inert as a contact toxicant, actively kills sap-sucking forms such as aphids, on treated plants.

4) In the protected site a long-lasting toxic action which permits prophyllactic control of certain insects by treating seeds and seedlings.

5) Avoid the rapid flare of aphid, mite and coccid infestations noted after initially good kills by direct contact insecticides.
    a) It is to be remembered that every one of these "advantages" may be open to qualification in terms of any specific systemic toxicant.

PRECAUTIONS 2651

1) Clearly, for a toxicant absorbed by plants, the questions of residues, persistence of residues, toxic byproducts, concentration in particular plant parts or plant substances and lapse of time which must be allowed between plant treatment and harvest are problems each of which assumes an imperious form. Such a toxicant may be deemed safe (other things equal) if:
    a) The concentration in the plant at harvest is safe, negligible or non-hazardous.
    b) If the decomposition products (end-products) are harmless. For example the decomposition of OMPA in the plant is linear with time, the period for 90% degradation being (depending on conditions) 4 - 5 weeks in June - July treated crops, 4 - 5 weeks in August - September treated crops, several months in October - November treated crops. These facts suggest that activity of the plant's metabolism, growth rate, output of new foliage, etc., all influence the fate of the systemic toxicant within the plant.

SOME ESSENTIAL CONSIDERATIONS IN SYSTEMIC INSECTICIDE ACTION

1) Rate of penetration into the plant interior; variables: The toxicant, the plant, the physiological state or condition of the plant. (After Metcalf, R. L. [2231] quoting Refs. 694, 695, 2246, 2236.)

1) Rate of penetration into the plant interior; variables (Continued):

Time After Treatment (Hrs)	% Of Toxicant Total In Leaf-Interior Of Plant Shown			
	BFPO	OMPA		Systox® (thiono-isomer)
	Bean	Bean	Lemon	Lemon
1	16	7	6.8	5
5 - 6	20	38	18	19.6
24	28	69.5	43.9	14.7
72	25 (At 96 Hrs)	80.5	76.5	66.7

2) Absorption, translocation, metabolism of typical systemic toxicants after topical application to plants (Lemon) via the stem of 20 micro liters: 2246 2236

Time After Treatment (Days)	OMPA		Systox® (Thiono-Isomer)		Systox® (Thiol-Isomer)	
	ppm (Upper Leaves)	Partition* $HCCl_3$/N NaOH	ppm (Upper Leaves)	% Metabolism	ppm (Upper Leaves)	% Metabolism
1	153	21.7	0	-	67	70.5
2	375	13.8	88	71	708	90.5
4 - 5	546	15.6	304	97	1740	100
14	888	11.3	-	-	-	-
28	1515	7.5	-	-	-	-

*As an indication of decomposition, the breakdown products of OMPA being chloroform insoluble.

a) Compared to efficiency of stem or leaf penetration the absorption of some systemic toxicants by the roots may be relatively inefficient due to selective action of roots on materials absorbed and mechanical segregation and retention by the soil. However, via the roots, high concentrations may be obtained within the plant. Uptake may be more efficient from sand than from soil culture media, and may be most effective of all from water-culture media. 694 695 2246

Vicia faba (via roots)	163 μg/g leaf in 3 days from	0.05% sol. OMPA
" (")	127 μg/g leaf "	0.05% sol. BFPO
Lemon (Citrus) (")	309 ppm in leaf tissue in 4 weeks from	0.0059% sol. OMPA
" (")(")	210 " "	0.0059% sol. Systox® (thiono)
" (")(")	4500 " "	0.036% sol. OMPA

In Vicia 38% of total OMPA in the plant is in the leaves in 7 days after treatment, and in the lemon 69% is in the leaves at 47 days.

3) With regard to the minimum concentration of systemic toxicant which when applied to a plant, for example via the roots, will kill a given species of insect feeding upon the plant, the variables again are the toxicant and its essential toxicity, the plant and its condition and the insect species to be killed. For example, in terms of minimum concentration to kill Aphis fabae, feeding on Vicia faba, of various systemic insecticides: OMPA = 0.005%, sodium fluoroacetate = 0.0002%, BFPO = 0.002%, nicotine = 0.01%, para-oxon = 0.04%. 695 702 703

4) Translocation: Influenced by species of plant, its physiological state, age, condition, etc. Rate of accumulation in the plant of a toxicant is, among other things, a function of its solubility in water, its stability to chemical and metabolic alteration and its vapor pressure (for instance highly volatile systemics may rapidly leave the plant via the transpiration stream).

a) The direction of translocation from the application site is, in general, upward toward the rapidly growing parts of the plant. For example, of OMPA taken up by young lemon plants 12.7% was to be found in basal parts, 22.3% in median parts, 65% in terminal parts of plant; in case of Systox® the concentration of the total respectively in the 3 sites was: 23.5%, 35.2%, 41.3%. 2231

b) In the case of effective systemic toxicants translocation distance is great. Mature trees (consult BFPO) have been protected from mite and insect attack by applications at the base of the trunk.

c) Important it is to consider stability of a given toxicant in the treated plant and the rate of the metabolic breakdown, as well as to consider whether the metabolic breakdown at once detoxifies the systemic agent or produces toxic intermediates in some instances (with OMPA) more toxic by far (1,000,000 fold) than the parent substance.

5) Metabolism of systemic insecticides in plants:

a) It is well known that some toxicants of the organic phosphorus category are transformed in the animal body and by in vitro biochemical systems (tissues, tissue slices) into substances more effective than the parent in anti-choline esterase activity and thus, generally speaking, of greater toxicity than the parent compound.

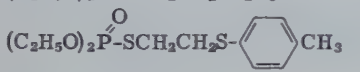
(1) Among these toxicants is OMPA, the monophosphoramide oxide of which is 1,000,000 times more active in anti-cholinesterase activity than OMPA itself. Evidence has been offered that in the case of OMPA a transformation, in all respects similar to that which takes place in animals, occurs in plants. 497 859

(2) It is less clear for OMPA whether the monophosphoramide oxide is the agent of systemic activity. The transformation in plants is slow and the monophosphoramide oxide is highly labile and subject to rapid degradation. Thus, the systemic action of OMPA against insects may well be that of the parent substance with the activation to monophosphoramide oxide occurring in the insect and not in the plant body. 1416 2246 2507

b) In the case of Systox® both the thiol- and the thiono-isomer are taken up by plants (although the thiol- 1468
form is far more effectively and rapidly absorbed) and there altered metabolically to yield at least three 2236
highly toxic, non-ionic substances with high effectiveness as choline esterase inhibitors. These products 1072
undoubtedly play a major role in the systemic insecticidal action of Systox®. The products of the degre- 1073
dation of the intermediates in plants are non-toxic substances, i.e. diethyl phosphoric acids and thiol- 3092
alcohols.

SOME EXAMPLES OF COMPOUNDS AND CLASSES OF COMPOUNDS GIVING EVIDENCE OF HIGH SYSTEMIC INSECTICIDAL ACTIVITY

1) Compounds of dialkyl thiophosphoric esters with thioglycol ethers yield effective contact insecticides with high systemic effect; these compounds have led to Systox® and thence to selenolphosphoric acid esters which are intensely active systemic toxicants (though with a high residue hazard). 1130

Compound	B.P. (°C)	LC_{100} For Aphis (%)	Subcutaneous Toxic Dose, Mouse, mg/k
	Thiophosphoric Acid Esters Of Thioglycol Ethers		
$(CH_3O)_2\overset{S}{P}-OCH_2CH_2SCH_3$	108° at 2 mmHg	0.005	200
$(C_2H_5O)_2\overset{S}{P}-OCH_2CH_2SCH_3$	119 at 2 mmHg	0.005	25
$(C_2H_5O)_2\overset{S}{P}-OCH_2CH_2SC_2H_5$	128 at 1.2 mmHg	0.001	25
$(C_2H_5O)_2\overset{S}{P}-OCH_2CH_2SC_3H_7(n)$	139 at 2 mmHg	0.005	50
$(C_2H_5O)_2\overset{S}{P}-OCH_2CH_2SC_4H_9(n)$	161 at 3 mmHg	0.001	25
$(C_2H_5O)_2\overset{S}{P}-OCH_2CH_2SC_5H_{11}(n)$	147 at 2 mmHg	0.005	50
	Thiophosphoric Acid Esters		
$(CH_3O)_2\overset{O}{P}-SCH_2CH_2SCH_3$	83 at 0.07 mmHg	0.001	100
$(C_2H_5O)_2\overset{O}{P}-SCH_2CH_2SCH_3$	135-140 at 4 mmHg	0.0005	2.5
$(C_2H_5O)_2\overset{O}{P}-SCH_2CH_2SC_2H_5$	128 at 1 mmHg	0.0005	10
	Not distillable	0.05	500
	Selenolphosphoric Acid Esters		
$(C_2H_5O)_2\overset{O}{P}-Se(CH_2)_2SCH_3$	152 at 3 mmHg	0.005	5
$(C_2H_5O)_2\overset{O}{P}-Se(CH_2)_2SC_2H_5$	153 at 3 mmHg	0.0005	10

2) 0,0-Dialkyl S-alkyl thiomethyl phosphorodithioates: Systemic activity of $(RO)_2\overset{S}{P}-S-CH_2SR'$ compounds vs. Tetranychus bimaculatus on excised bean plants. Most promising have R,R' = ethyl and R = ethyl, R' = isopropyl. As 50% activated carbon seed treatments have been found effective vs. early season cotton pests. 548

a) Systemic action vs. mites on cut 2-leaf bean plants in test solutions, with fumigant action by direct vapor action of the solutions prevented:

R	R′	LD_{50} mg/k Mouse, ip	% Kill T. bimaculatus At			
			100 ppm	10 ppm	5 ppm	1 ppm
CH_3	C_2H_5	4 - 16	100	92	91	82
CH_3	iso-C_3H_7	4 - 16	100	94	85	67
CH_3	C_3H_7	8 - 32	100	100	81	0
CH_3	$CH_2=CHCH_2$	16 - 64	100	100	95	0
CH_3	$(CH_3)_3C$	16 - 64	85	0	0	0
CH_3	$(CH_3)_2CHCH_2(CH_3)_2C$	-	99	19	0	0
CH_3	$C_{12}H_{15}$	-	0	0	0	0
C_2H_5	C_2H_5	1 - 4	100	100	100	100
C_2H_5	iso-C_3H_7	4 - 16	100	100	100	98
C_2H_5	C_3H_7	16 - 32	100	100	100	55
C_2H_5	$CH_2=C-CH_2$	4 - 16	100	100	69	30
C_2H_5	$(CH_3)_3C$	1 - 4	97	63	0	0
C_2H_5	C_5H_7	-	100	90	-	-
C_2H_5	tert-C_7H_{15}	16 - 32	93	0	-	-
C_2H_5	C_8H_{17}	-	30	0	-	-
C_2H_5	$C_{12}H_{25}$	-	0	-	-	-
iso-C_3H_7	C_2H_5	64 - 256	100	93	33	0
iso-C_3H_7	iso-C_3H_7	64 - 256	100	100	80	13
iso-C_3H_7	C_3H_7	128 - 256	100	83	-	31
iso-C_3H_7	$CH_2=CHCH_2$	16 - 64	100	100	28	0

2) a) Systemic action vs. mites on cut 2-leaf bean plants in test solutions, with fumigant action by direct vapor action of the solutions prevented (Continued):

R	R′	LD_{50} mg/k Mouse, ip	% Kill *T. bimaculatus* At			
			100 ppm	10 ppm	5 ppm	1 ppm
iso-C_3H_7	tert-C_4H_9	64 - 256	100	0	-	-
C_3H_7	C_2H_5	64 - 256	100	0	0	0
C_3H_7	iso-C_3H_7	128 - 512	98	0	0	0
C_3H_7	C_3H_7	128 - 256	99	0	0	0
C_3H_7	$CH_2 = CHCH_2$	64 - 128	100	0	0	0
C_3H_7	tert-C_4H_9	64 - 256	3	0	-	-
C_3H_7	tert-C_4H_9	-	0	-	-	-

3) Field tests of systemic insecticides on vegetable crops: Mortality of aphids and mites on mature egg-plant following insecticidal applications; aphids = *Myzus persicae*, *Illinoia solanifolii*; mites = *Tetranychus bimaculatus*: 838

Compound	Emulsion Strength (%)	Pints/100 gals	% Mortality Of		
			Aphids (2nd day)	Mites (2nd day)	Mites (5th day)
Systox®	32	1.5	100	99.2	99.9
"	32	1.0	100	99.2	99.2
"	32	0.5	100	96	98.9
"	32	0.25	100	91.5	98.0
Malathion	50	1.0	100	89.8	93.9
OMPA	45	1.0	98	67.3	93.0
"	45	1.5	98	65.6	86.4
Parathion	25	1.0	100	96.1	99.4

a) Young egg plant sprayed 3 times in July at 10-day intervals with various concentrations of Systox® and OMPA lost toxicity quite rapidly; still OMPA at 4:100 and Systox® at 1:100 yielded 80 - 90% aphid control 24 days after last spraying and 40 - 60% mite control 2 months after last spray. Systox® yielded good initial kills of *Empoasca fabae* in concentrations to 0.25 pints per 100 gals., but OMPA was ineffective. OMPA and Systox® controlled *Tetranychus bimaculatus*, *Rhophlosiphum pseudobrassicae*, *Myzus persicae*, *Illinoia solanifolii*.

b) Systox®, parathion and malathion used to control *Pseudococcus brevipes* on pineapple as contact insecticides, were not systemically translocated to older parts of the plant in toxic quantity sufficient to control mealy-bugs on the underground or leaf-base portions of the plant, or colonies established on plant butts. Satisfactory as contact sprays, but with little if any effect on subsurface colonies. 490

4) OMPA and Isopestox® in practical field use: 1267

a) Used on hops vs. *Phorodon humuli*, OMPA was affected, with respect to systemic uptake, by age of foliage; thus, 0.6 lb per acre (0.6 k per hectare) initially, must be followed by 1.3 lbs per acre applied when plants are at full height.

b) OMPA vs. *Pentatrichopus fragaefolii*: 1 lb per acre in mid-May, repeated in June on non-fruiting plants; for fruiting plants one spray only in April. Persistence affected by rate of plant growth, enduring 2 - 3 weeks in July to more than 15 weeks after November treatment. 0.75 lb per acre controlled *P. fragaefolii*, but not *Amphophora rubi*, *Macrosiphum rosae*, *M. euphorbiae* which required at least 7 lbs per acre for control. Yielded complete control in 8 days of *Myzus persicae* and *Macrosiphum gei* on tulips at 0.3% concentration (spray) or at 100 cc of 0.3% solution per 500 g soil by soil watering.

c) Vs. *Tetranychus telarius* on *Hydrangea*:

Compound	Method	Concentration (%)	% Mortality
OMPA	Soil watering	0.1	56
Isopestox®	"	0.05	99
OMPA	Spraying	0.1	75.5
Isopestox®	"	0.05	98.5

(1) The effect of OMPA on mites compared unfavorably with that of Isopestox®.

5) Sodium fluoroacetate, para-oxon, OMPA and Isopestox® evaluated vs. eggs and larvae of *Pieris brassicae*: 703

a) OMPA exercised little toxic action on *Pieris*.

b) Para-oxon, Isopestox®, Sodium fluoroacetate were active by contact and when uptaken by cabbage via roots from soil and from solution culture; sodium fluoroacetate, and particularly para-oxon, showed effective systemic action following application to leaves.

c) In order of decreasing toxicity: Para-oxon > sodium fluoroacetate > Isopestox® > OMPA.

d) Para-oxon alone was outstandingly toxic to *Pieris* eggs and larvae; watered on soil at roots of cabbage, it killed larvae in the egg batches on leaves. Death came during larval egg-emergence. 20 cc of a solution containing 0.001 cc of para-oxon on 400 g moist soil, containing a cabbage plant 6 - 8 inches high and with 6 - 8 leaves, yielded 95% kills of eggs and 100% kills of larvae which succeeded in hatching; 20 cc of a 0.002 cc para-oxon-containing solution yielded 100% kill systemically of 3rd instar larvae.

6) OMPA, Dimefox, Para-oxon and Sodium fluoroacetate vs. *Phaedon cochleariae*, compared by direct contact technique and by systemic action (foliage dipped in toxicant solutions then dried): 704

a) Contact order of toxicity: Para-oxon > sodium fluoroacetate = dimefox > OMPA (adult more resistant than larva).

b) Systemic effectiveness order: Para-oxon > dimefox > sodium fluoroacetate = OMPA; the first 2 yielded complete kills at practical concentrations. Vs. Phaedon OMPA and sodium fluoroacetate were systemically ineffective.

Compound	Approximate Amounts To Yield 100% Kills					
	Dipping (% Concentration)			Systemically Via Soil cc/pot *		
	Aphis	Pieris	Phaedon	Aphis	Pieris	Phaedon
OMPA	.05	> .2	>1.0	.02	> .04	> .1
Dimefox	.05	> .1	> .5	.002	> .02	.01
Sodium fluoroacetate	.001	> .1	> .1	.001	.02	> .1
Para-oxon	.0005	.01	.01	> .04 g	.002 g	.002 g

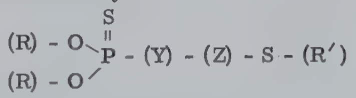
*Pots of 3½ inch diameter with 400 grams compost.

7) Action of sodium fluoroacetate, OMPA, BFPO and Para-oxon vs. aphids:
   a) All were toxic by dipping method in the order: Para-oxon > sodium fluoroacetate > OMPA = > BFPO.
   b) By systemic action, root application the order of toxicity:
      Sodium fluoroacetate > BFPO > OMPA = para-oxon (solution culture);
      Sodium fluoroacetate > BFPO > OMPA > para-oxon (sand, soil culture).
      (1) Safety margin between insecticidal and phytotoxic concentrations were greater with sodium fluoroacetate than with others. Systemic activity was readily demonstrable for sodium fluoroacetate, with difficulty for OMPA and not at all with BFPO or para-oxon. Only BFPO had a fumigant effect, either of itself or after plant absorption. Treated plants yielded an insecticidal vapor which was itself systemically active for untreated plants. Para-oxon was the most phytotoxic, while OMPA was the most persistent, at the lowest concentrations yielding 100% kills. Sodium fluoroacetate proved an extremely effective systemic aphicide via leaves or roots of Vicia faba, was not phytotoxic at several times the concentration needed for insecticidal action but proved too generally toxic for practical use.

ADDENDUM TO GENERAL TREATMENT OF SYSTEMIC INSECTICIDES

Chemical structure and insecticidal activity of some systemic insecticides for Macrosiphum sanborni: 1705

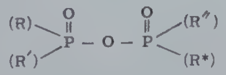
General Formula:



$$(R)\text{-}O\text{-}\overset{\overset{S}{\|}}{P}(\text{-}O\text{-}(R))\text{-}(Y)\text{-}(Z)\text{-}S\text{-}(R')$$

Compound (Thiophosphates)	(R)	(Y)	(Z)	R′	Designation	Contact Action LC₅₀ (% Technical)	Contact Action 5% Fiducial Limits At LC₅₀	Systemic Action LD₅₀ (lbs(tech)/1000ft²)	Systemic Action 5% Fiducial Limits At LD₅₀
O,O-Diethyl-O-ethylmercaptoethyl thiophosphate (Demeton)	C_2H_5 -	-O-	C_2H_4 -S-	C_2H_5	E-1059	0.006	.004 - .008	0.007	.003 - .013
O,O-Diethyl-O-methylmercaptoethyl thiophosphate	C_2H_5 -	-O-	C_2H_4 -S-	CH_3	21/83	.007	.004 - .011	.005	.002 - .010
O,O-Diethyl-Se-ethylmercaptoethyl selenothiophosphate	C_2H_5 -	-Se-	C_2H_4 -S-	C_2H_5	20/58	.002	.001 - .004	.003	.001 - .008
O,O-Diethyl-Se-methylmercaptoethyl selenothiophosphate	C_2H_5 -	-Se-	C_2H_4 -S-	CH_3	20/86	.003	.002 - .006	.001	.001 - .002
O,O-Diethyl-O-ethylmercapto-n-propyl thiophosphate	C_2H_5 -	-O-	C_2H_4 -S-	C_2H_5	21/125	.020	.010 - .055	.302	.245 - .363
O,O-Diethyl-O-ethylmercaptoisopropyl thiophosphate	C_2H_5 -	-O-	CH_2-CH_2 -S- CH_3	C_2H_5	E-1486	.009	.005 - .016	.023	.017 - .032
O,O-Diethyl-O-ethylmercapto-n-butyl thiophosphate	C_2H_5 -	-O-	C_4H_8 -S-	C_2H_5	E-1484	.012	.001 - .204	.105	.058 - .174
O,O-Diethyl-O-n-butylmercaptoethyl thiophosphate	C_2H_5 -	-O-	C_2H_4 -S-	C_4H_9	E-1492	.015	.009 - .027	.065	.032 - .115
O,O-Diethyl-O-n-hexylmercaptoethyl thiophosphate	C_2H_5 -	-O-	C_2H_4 -S-	C_6H_{13}	E-1495	.021	.015 - .029	.098	.047 - .251
O,O-Diethyl-O-carbethoxymethylethyl thiophosphate	C_2H_5 -	-O-	$C_2H_4\text{-S-}CH_2C(=O)\text{-O-}$	C_2H_5	E-1531	.214	.123 - .372	1.95	1.15 - 3.89

General Formula:



(Pyrophosphates)	(R)	(R′)	(R″)	(R*)	Designation	LC₅₀ (% Technical)	5% Fiducial Limits At LC₅₀	LD₅₀ (lbs(tech)/1000ft²)	5% Fiducial Limits At LD₅₀
Tetraethyl pyrophosphate (TEPP)	C_2H_5 -O-	C_2H_5-O-	C_2H_5-O-	C_2H_5-O-	TEPP	0.007	.005 - .010	7.94	1.0 - 63.1
Dimethylamido triethyl pyrophosphate	$(CH_3)_2$ =N-	C_2H_5 -O-	C_2H_5-O-	C_2H_5-O-	M 2/34	.025	.019 - .033	.022	.013 - .033
Bis-(dimethylamido) diethyl pyrophosphate (asym.)	$(CH_3)_2$ = N-	$(CH_3)_2$ =N-	C_2H_5-O-	C_2H_5-O-	15/8b	.058	.023 - .115	.038	.015 - .076
Bis-(dimethylamido) diethyl pyrophosphate (sym.)	$(CH_3)_2$ = N-	C_2H_5-O-	$(CH_3)_2$= N-	C_2H_5-O-	15/8	.090	.082 - .099	.063	.060 - .066
Tris-(dimethylamido) monoethyl pyrophosphate	$(CH_3)_2$ = N-	$(CH_3)_2$ =N-	$(CH_3)_2$ =N-	C_2H_5-O-	M 2/35	.302	.219 - .407	.096	.066 - .145
Bis-(bis-dimethylamido) pyrophosphate (OMPA)	$(CH_3)_2$ =N-	$(CH_3)_2$ = N-	$(CH_3)_2$ =N-	$(CH_3)_2$ =N-	13/163	.550	.389 - .776	.129	.081 - .204

Interpretations:

Thiophosphates:

1) Compounds with a P-Se-C link in one group were more effective contact and systemic agents than analogues with a P-O-C linkage.
2) Increase in side-chain length beyond -C-C- on either side of S-linkage decreased effectiveness.
3) Isopropyl brought less change in effectiveness than n-propyl or higher alkyl-groups.
4) A methyl group beyond the S-linkage tended to be less effective than ethyl by contact but more effective by systemic action.

Pyrophosphates:

1) Stepwise replacement of ester-groups by dimethylamido-groups led to decrease in both contact and systemic action and hydrolysis rate.
2) TEPP failed as a systemic insecticide because of its instability to hydrolysis.
3) Rate of hydrolysis of TEPP and its derivatives containing one and two asym-dimethylamido-groups was rapid enough to preclude practical use of these compounds as systemic insecticidal agents.

173

TEMPERATURE AND INSECTICIDAL ACTION

1) SOME TABULAR, QUANTITATIVE DATA

a) Temperature and the toxicity of certain inorganic stomach poison insecticides; insects: Anticarsia gemmatilis, Prodenia eridania 5th instar larvae; oral administration: 943

Insecticide	°F	Anticarsia gemmatilis			Prodenia eridania		
		Dosage Range (mg/g)	Mean Survival (hrs.)	LD_{50} (mg/g)	Dosage Range (mg/g)	Mean Survival (hrs.)	LD_{50} (mg/g)
Cryolite (synthetic)	80	(0.08-0.18)	38	0.13	(0.38-1.01)	27	0.55
" "	60	(.08- .22)	42	.13	(.19- .55)	45	.33
Acid lead arsenate	80	(.07- .15)	31	.11	(.07- .28)	19	.14
" " "	60	(.04- .13)	40	.06	(.07- .14)	37	.09
Calcium arsenate	80	(.05- .19)	36	.10	(.09- .26)	20	.16
" "	60	(.03- .15)	42	.06	(.03- .13)	28	.07
Basic copper arsenate	80	(.06- .26)	29	.14	(.09- .19)	22	.13
" " "	60	(.04- .16)	42	.11	(.07- .15)	28	.10

b) Toxicity of various insecticides and holding temperature after treatment; Blatta germanica adult ♀♀. Topical application, to the sternum, of insecticides in dioxane solution. Mortality readings taken at 5 days after treatment. 1305

Insecticide	LD_{50} (μg/insect) 5 Days At Holding Temperature Shown		
	32°C	22°C	14.5°C
DDT	40.8 ± 2.2	12.9 ±2.2	2.1 ±0.31
Pyrethrins	1.45±0.23	0.8 ±0.23	0.32±0.23
Lindane	0.18±0.02	0.1 ±0.02	0.071 ± 0.02
Aldrin	0.4 ±0.22	0.57±0.22	1.36 ± 0.22
Dieldrin	0.22±0.02	0.35±0.02	1.1 ± 0.02
Dioxane Control (Dosage 1 cc dioxane)	3.5% mortality	1% mortality	1% mortality

c) Effect of atmospheric environment (temperature and humidity) on toxicity of contact poisons for Tribolium castaneum adults; insecticides applied as contact sprays; pyrethrins, lauryl thiocyanate, nicotine in aqueous medium; DNOC in ethylene glycol; DDT in Wakefield half-white oil: 2532

(1) Pyrethrins, and pyrethrins + terpineol, LC_{50} % (w (total pyrethrins/v)

Treatment		Terpineol	LC_{50} % (w/v)	
Before Spraying	After Spraying	[+(present); 0(absent)]	Experiment I	Experiment II
Cold (60°F, RH 48-56%)	Cold	0	0.0044	0.0031
Hot (80°F, RH 60%)	Cold	0	.0049	.0033
Cold	Hot	0	.0092	.0098
Hot	Hot	0	.0116	.0156
Cold	Cold	+	.0027	.0018
Hot	Cold	+	.0045	.0018
Cold	Hot	+	.0122	.0110
Hot	Hot	+	.0198	.0125

(2) Lauryl thiocyanate in 20% acetone (v/v) + 0.1% sulfonated Lorol®:

Treatment Before Spraying Cold = 56-59°F, RH 50% Hot = 80.6°F, RH 52%	Treatment After Spraying		
	Cold LC_{50} % (v/v)	Hot LC_{50} % (v/v)	LC_{50} Mean % (v/v)
Cold	0.172	0.231	0.199
Hot	0.153	0.247	0.195
(Mean)	0.163	0.239	0.197

(3) Nicotine alkaloid in 20% Acetone (v/v) + 0.1% sulfonated Lorol®:

Treatment Before Spraying Cold = 56-60°F, RH 50-62% Hot = 80.6°F, RH 58-64%	Treatment After Spraying		
	Cold LC_{50} % (v/v)	Hot LC_{50} % (v/v)	LC_{50} Mean % (v/v)
Cold	0.297	0.288	0.292
Hot	.229	.365	.289
(Mean)	.260	.324	.291

(4) DNOC in ethylene glycol:
Cool storage post-treatment (58°-60°F) LC$_{50}$ %(w/v) = 0.67
Hot " " " (80.6°F) LC$_{50}$ % (w/v) = 0.98

(5) Highly refined white oil spec. gravity 0.88 at 15.5°C, 10% distilling at 298-319°C, 80% at 319-388°C, unsulfonatable residue = 88% v/v; to be considered a chemically inert substance:
Cool storage post-treatment (58°F) LD$_{50}$ = 4.03 cc
Hot " " " (80°F) LD$_{50}$ = 3.51 cc

(6) DDT in solution in the above-described refined oil:
Hot storage post-treatment (80°F) LC$_{50}$ % (w/v) = 0.95
Cold " " " (65°F) LC$_{50}$ % (w/v) = 0.36

(7) Potency under cold storage as a proportion of the potency under hot storage for several insecticides considered above:

Insecticide	Medium	Cold Before Treatment	Cold After Treatment	Cold Before And After Treatment
Pyrethrins	Aqueous (2 experiments)	1.19; 1.31	2.25; 3.84	2.67; 5.01
Pyrethrins + terpineol	" " "	1.07; 1.62	4.45; 6.49	6.90; 7.21
Lauryl thiocyanate	"	0.98	1.47	1.43
Nicotine	"	0.99	1.24	1.23
DNOC	Ethylene glycol	—	—	1.46
DDT	Wakefield Half-White Oil	—	—	2.61
Wakefield Half-White Oil	—	—	—	0.87

d) Effects of temperature and humidity on the toxicity of certain insecticides for Anthonomus grandis (adult); contact dusting on cotton plants: 1101

(1) Tests on field gathered insects; mortality readings cumulative over 5 days:

Insecticide	85°F, RH 80%		85°F, RH 70%		85°F, RH 45%	
	Lbs./acre	% Kill	Lbs./acre	% Kill	Lbs./acre	% Kill
Calcium arsenate	6	0	4	21.8	1	13.3
" "	10	47.3	6	47.4	2	52.8
" "	14	54.9	8	56.4	3	66.2
" "	16	71.4	10	46.2	4	66.2
20% Toxaphene® in Sulfur	14	14.2	2.5	12.2	4	38.1
" " " "	16	50.8	5	36.1	6	35.6
" " " "	24	22.2	8	45.6	8	39.8
" " " "	—	—	10	50.3	14	32.3
20% Chlordane in Sulfur	15	4.8	2.5	11.0	4	22.1
" " " "	16	23.8	4	26.0	6	32.3
" " " "	24	0.7	6	34.2	8	31.5
" " " "	—	—	8	24.8	10	36.6

(2) LD$_{50}$ as Lbs./acre for Anthonomus grandis:

Insecticide	Laboratory Reared Insects				Field Collected Insects			
	Laboratory Test 84-92°F,RH.44-63%		Field Test 73-107°F,RH 24-90%		Laboratory Test 78-93°F,RH 34-70%		Greenhouse Test 76-108°F,RH 27-87%	
	LD$_{50}$	Regression Coeff.	LD$_{50}$	Regression	LD$_{50}$	Regression	LD$_{50}$	Regression
Calcium arsenate	2.2	2.7	2.5	3.0	5.4	4.5	2.0	0.6
20% Toxaphene® in Sulfur	1.9	3.9	3.7	2.4	4.4	4.7	3.9	0.4
3% Lindane, 5% DDT in Sulfur	2.2	2.5	9.1	2.0	8.6	4.7	7.5	3.0
10% Chlordane in Sulfur	2.8	2.3	**		18.0	1.4	23.1	1.0
10% Chlordane in Sulfur *	—	—	—	—	27.6	1.7	49.1	1.5

*Insects placed on plants 24 hrs. after dusting.
**Dosages to 12 lbs./acre yielded only 36% mortality.

e) Effect of temperature on the toxicity of Malathion, and Malathion-Piperonyl butoxide 1 : 10 to DDT-R and DDT-non-R biotypes of Musca domestica (4 day old ♂ adults); topical application in acetone solutions; mortality readings at end of 24 hrs.: 2575

Temperature (°F)	Campus Biotype DDT-R						KUN Biotype DDT-non R					
	Malathion			Malathion + PBO			Malathion			Malathion + PBO		
	LD$_{50}$ ug/g	FL 95%*	Slope	LD$_{50}$ ug/g	FL 95%	Slope	LD$_{50}$ (μg/g)	FL 95%	Slope	LD$_{50}$ μg/g	FL 95%	Slope
63	30.12	26.85-33.65	6.23	50.79	38.02-62.81	3.25	18.80	18.39-20.53	9.22	34.66	30.89-45.58	6.04
70	26.44	22.34-27.33	7.24	38.56	34.44-43.55	5.74	17.57	13.81-17.62	15.87	24.54	23.52-28.11	8.49
75	20.75	19.41-21.63	12.41	30.71	27.38-34.28	5.85	12.87	11.93-13.43	10.92	18.83	16.7 -26.66	3.15
82	19.56	17.86-23.88	4.48	34.66	31.99-37.76	7.97	13.39	12.63-14.79	8.26	19.43	17.32-21.38	7.62

* = Fiducial Limits 95% level.

2) SUMMARY DATA ON EFFECT OF TEMPERATURE ON INSECTICIDE TOXICITY

For review also consult Ref. 1755.

Rotenone: Ahasverus: Immersion in Derris extract 5 times more toxic at 25°C than at 10°C. 637
Melophagus: More rapid penetration of cuticle at 30°C than at 20°C; mortality higher at higher temperature. 353
Ahasverus: Immersion in Derris extract gave higher mortality at 20°C than at 25°C pre- and post-treatment. 637
Apis mellifera: Oral or topical; mortality higher at 20°C than at 34.5°C post-treatment temperature. 296
Lymantria (larvae) Given LD; death more rapid at 30°C than at 20°C post-treatment temperature; although time of death is later at lower temperature eventual mortality is higher. 1822

Pyrethrum:
Euttetix: Equivalent spray doses: At 100°F 73% kill; at 60°F 53% kill. 1402
Galleria (larva): by injection: Twice more effective at 30°C than at 20°C. 213
Euttetix: Equivalent spray doses: Mortality at 60°F post-treatment = 81-88%; at 100°F = 29-33%. 1402
Apis mellifera, oral, contact: Mortality higher at 20°C than at 34.5°C post-treatment temperature. 296
Musca domestica: Lower % recovery at 20°C post-treatment temperature than at 38°C. 890
Tribolium: Topical, at 60°F post-treatment more toxic than at 80°F by 4-7 times. 296
Blattella, topical: More toxic at lower than at higher post-treatment temperatures. 1305

DNOC:
Lymantria monacha, topical: Susceptibility of larvae higher with gradually increasing temperatures. 1569
Tribolium topical: More toxic at 60°F post-treatment than at 80°F by 1.5 times.

DDT:
Musca domestica: 40 minutes exposure to residual deposits at 95°F gave 100% death; at 65°F some survived. 2010
Musca domestica: In continuous exposure to residual deposits, more mortality at 70°F than at 90°F. 1561
Musca domestica, exposed to residual films at 65°F: Mortality greater at 70°F post-treatment than at 100° F. 2010
Plutella (larvae), sprayed with 0.0125% DDT: 9% mortality at 90°F, 78% at 70°F post-treatment temperature. 879
Macrocentrus, exposed to residues: Higher mortality and more rapid death at < 70°F post-treatment than at > 80°F. 2491
Tribolium, topical: More toxic at 60°F post-treatment than at 80°F by 2.5 times. 296
Blattella; topical: More toxic at lower than at higher post-treatment holding temperatures. 1305

Lethane®:
Musca domestica: Less % recovery at 20°C post-treatment temperature than at 38°C. 890

Lauryl thiocyanate:
Tribolium, topical: More toxic at 60°F post-treatment temperature than at 80°F by 1.5 times. 296

Nicotine:
Tribolium, topical: Equal toxicity at low and high post-treatment holding temperatures. 296
Apis mellifera, oral: Proved less toxic at 60°F post-treatment temperature than at 80°F. 296

Calcium arsenate, Acid lead arsenate, Copper arsenate:
Prodenia, Anticarsia (larvae): Oral toxicity at 60°F post treatment more by 2 times than at 80°F; mortality develops later at the lower temperature. 943

Carbon disulfide, Chloropicrin, Ethylene dichloride (fumigants):
Tribolium confusum, fumigant efficacy higher with temperature from 10°-35°C for adults, eggs and for adults higher below 10°C. 3013,2816

Fumigants:
Tetranychid acarines: Toxicity shows pronounced rise with increasing temperature. 2705

Lindane:
Blattella germanica, topical: More toxic at lower than at higher post-treatment temperatures. 1305

Parathion:
Musca domestica, continuous exposure to residues: Higher mortality at 90°F than at 70°F. 1561
Tetranychid acarines: pronounced rise in toxicity with increasing temperatures. 2705

Aldrin:
Blattella germanica, topical: More toxic at higher than at lower post-treatment temperatures. 1305
Musca domestica, exposed to residues: Higher mortality at 90°F than at 70°F. 1561

Dieldrin:
Blattella germanica, topical: More toxic at higher than at lower post-treatment temperatures. 1305
Musca domestica, exposed to residues: Higher mortality at 90°F than at 70°F. 1561

Chlordane:
Musca domestica, exposed to residues: Greater mortality at 90°F than at 70°F. 1561

Toxaphene®:
Musca domestica, exposed to residues: Higher mortality at 90°F than at 70°F. 1561

DDD:
Musca domestica, exposed to residues: Greater mortality at 70°F than at 90°F. 1561

Methoxychlor:
Musca domestica, exposed to residues: Greater mortality at 70°F than at 90°F. 1561

174

TERMITES (REPELLENTS AND INSECTICIDES FOR)

I) Length of time during which samples of a wood most susceptible to termite attack were protected from Cryptotermes brevis by 10 minute submersions in solutions of the listed compounds: 3352

Compound	% Concentration	Results Wood Uneaten For:
Copper pentachlorophenate	0.1	4 years
Sodium pentachlorophenate	0.2	3 years 10 months
Ferric dimethyldithio carbamate (Fermate)	0.5	4 years 8 months
Copper dimethyldithio carbamate	0.5	> 2 years
Zinc dimethyldithio carbamate	0.5	> 2 years
α-Naphthoflavone	0.5	3 years 3 months
Xanthone	0.5	3 years 3 months
Pyridylmercuric chloride	0.5	3 years
Pyridylmercuric stearate	0.5	3 years
Zinc Lake (acetic acid) Chrysazin	0.5	2 years
Hexachlorophenol	1.0	4 years
Pentabromophenol	1.0	4 years
Diphenyl mercury	1.0	3 years 7 months
Phenyl mercuric chloride	1.0	3 years 7 months
β-Methylanthraquinone (Tectoquinone)	1.0	3 years 3 months
Zinc Lake (acetic acid) Quinizarin	1.0	2 years
Zinc Lake (acetic acid) β-Chloroanthraquinone	1.0	2 years
Genicide acids (Xanthone mftr by-products)	1.0	1 year 7 months
4,6-Dinitro-o-sec.-butylphenol	1.0	1 year 2 months
Piperonyl cyclohexenone	1.0	1 year
DDT	2.0	4 years 9 months
Pentachlorophenol	2.0	4 years 9 months
Triphenyl stibine	2.0	3 years 7 months
Triphenyl phosphite	2.0	3 years 3 months
Diphenyl selenium	2.0	1 year 9 months
2,4-Dichlorophenyl potassium monochloracetaldehyde sulfonate	2.0	1 year 8 months
1,1-Diphenyl-(4-hydroxy-3,5-dichloro)-2,2,2-trichloroethane	2.0	> 1 year 5 months
Chlorinated anacardic acid	5.0	4 years
Tetrachlorophenol	5.0	4 years
Chlorinated crude cardol	5.0	3 years 6 months
Lindane	0.01	> 4 months
Lindane	1.0	ca. 1 year
Ryanodine	0.02*	at least 4 months
Chlordane	0.5 **	ca. 2 months
Chlordane	1.0 ***	> 1 year

* Immediately toxic to termites; repellent at least 4 months.
** Toxic for a few days; after 2 months wood eaten with impunity.
*** Wood not eaten until more than 1 year after treatment.

II) Days, after 10 minute submersion, before attack by Cryptotermes brevis; used: A wood most susceptible to attack: 3353

Compound	Dilutions Used (%) And Days Before Attack 0.01%	0.02%	0.05%	0.1%	0.2%	0.5%	1%	2%
Pinosylvin	Toxic for 2 months; not definitively attacked in 5 months.							
Stilbene	Toxic for 2 weeks; not definitively attacked in 4 months.							
Ryania	204; not definitively attacked in 18 months.							
Copper pentachlorophenate	27	42	108	111 (uneaten for ca. 7 years)				
Chlordane	—	—	20	22	25	48	373	378
Dieldrin	—	201	237	377	473	uneaten at 22 months.		
Aldrin	—	289	363	415	572	" " " "		
DDT	—	—	25	27	29	35	37	uneaten in 7 yr.
Butyl-DDT	—	49	51	79	114	119	120	(end)
DFDT	—	7	50	58	151	157	161	(end)

II) Days, after 10 minute submersion, before attack by Cryptotermes brevis; used: A wood most susceptible to attack: (continued) 3353

Compound	0.01%	0.02%	0.05%	0.1%	0.2%	0.5%	1%	2%
	Dilutions Used (%) And Days Before Attack							
Methoxychlor				uneaten at 1 year				
Dimethyl tetrachlorophthalate				uneaten at 18 months				
1,1-Di-(2-hydroxy-2,5-dichlorophenyl)-2,2,2-trichloroethane			36	uneaten at 9 months				
1,1-Di-(4-hydroxy-2,5-dichlorophenyl)-2,2,2-trichloroethane			147	192	330	454	514 (end)	
1,1-Di-(2-hydroxy-2,5-dichlorophenyl)-2,2,2-trichloroethane			uneaten at 18 months					
BHC α,β isomers			4	5	7	10	14	44 (end)
BHC γ-isomer (Lindane)	136	141	147	189	249	259	393 (end)	
Prolan			74	83	240	uneaten at 10 months		
Bulan			84	uneaten at 10 months				
β-Chloroethyl-β′(p-tert. butyl phenoxy)-β-methylethyl sulfite			27	80	240	uneaten at 10 months		

III) Three year tests Vs. Reticulitermes flavipes in jars of treated soil; dilutions of 1 part insecticidally active ingredient with various soil quantities: Minimum dosages which have retained effectiveness for 3 years:* 1505

DDT	1 : 200 (only dilution tested)
DDD	1 : 1000
Methoxychlor	1 : 1000
Lindane	1 : 50,000
Chlordane	1 : 20,000
Pentachlorophenol	1 : 200
Sodium pentachlorophenate	1 : 1000 (data for 2 years only)
Toxaphene®	1 : 10,000
Parathion	1 : 5000 (data for 2 years only)

The following failed after the period indicated:

Lindane at 1 : 100,000 (weakening after 3 years)
Pentachlorophenol at 1 : 2000 7 months
Pentachlorophenol at 1 : 10,000 5 months
Pentachlorophenol at 1 : 20,000 2 months
Sodium pentachlorophenate at 1 : 10,000 4 months
Sodium pentachlorophenate at 1 : 5000 5 months
Sodium pentachlorophenate at 1 : 10,000 4 months
Toxaphene® at 1 : 20,000 6 months
Parathion at 1 : 10,000 2 months
Parathion at 1 : 25,000 1 month(s)
Paradichlorobenzene at 1 : 100 6 months
Paradichlorobenzene at 1 : 500 1 month
Paradichlorobenzene at 1 : 1000 1 month

* Not repellent action nor fumigant action but true contact toxicity.

175

2, 4, 5, 4′ - TETRACHLORODIPHENYLSULPHONE (Tedion V 18)

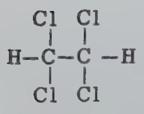
GENERAL

1) A product recently announced as an acaricide highly specific for phytophagous mites, but harmless to honeybees, and generally non-insecticidal. 1620
   a) Reported to kill all eggs and larvae of several harmful acarines, although adult forms were unaffected.
   b) No toxic effect on bees, flies, beetles or others exposed to dry films.
   c) Apparently non-phytotoxic.
   d) Large doses, orally to mice, produced no toxic effects.

176

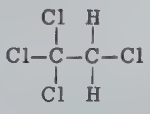
TETRACHLOROETHANE (Acetylene tetrachloride; Cellon; Bonoform)

N.B. 1,1,2,2-tetrachloroethane, $CHCl_2$-$CHCl_2$ is the symmetrical isomer; 1,1,1,2-tetrachloroethane CCL_3-CH_2Cl is the unsymmetrical isomer. The symmetrical form is ordinarily meant when the material is dealt with as an insecticide.



$$\begin{array}{c}\mathrm{Cl}\ \ \mathrm{Cl}\\ \mathrm{H-C-C-H}\\ \mathrm{Cl}\ \ \mathrm{Cl}\end{array}$$

(symmetrical isomer)



$$\begin{array}{c}\mathrm{Cl}\ \ \mathrm{H}\\ \mathrm{Cl-C-C-Cl}\\ \mathrm{Cl}\ \ \mathrm{H}\end{array}$$

(unsymmetrical isomer)

Molecular weight: 167.86

GENERAL

[Refs.: 353, 3199, 984, 2289, 396, 1059, 2815, 757, 162, 1210, 1801]

A substance which, while much less effective than hydrogen cyanide, methyl bromide or several nitriles, has found some use as a fumigant to control Cimex lectularius. Reported to be effective against clothes moths, being similar in toxicity to paradichlorobenzene. Effective, in closed spaces, against various wool-attacking insects. Occasionally used as a greenhouse and soil fumigant. Fungicidal, nematocidal and herbicidal toward some perennial weeds. More toxic than ethylene chloride vs. Cimex lectularius. Non-toxic in aerosols for Musca domestica.

PHYSICAL, CHEMICAL

[Refs.: 3199, 2221, 353]

Symmetrical: A colorless, refractive liquid of suffocating, chloroform-like odor, the inhaled vapors yielding a sweetish taste; not flammable; m.p. -36°C; b.p. 146.2°C; $d_{4°}^{20°}$ 1.6; wgt./gallon = 13.3 lbs.; 5.8 times as heavy as air in the vapor state; $n_D^{20°}$1.494; v.p. 11 mm Hg at 20°C; practically non-soluble in water (0.29 parts : 100 parts); miscible with alcohol, ether; solvent for fats, waxes, greases, oils, resins, gums, etc.; dissolves and/or damages rubber and rubber goods. Vapor pressures and maximum weight which can exist in vapor form in 1000 ft^3 chamber at various temperatures: 2671

Temperature (°F)	V.P. (mm Hg)	Lbs. As Vapor/1000 ft^3
32	1.4	0.9
59	4	2
68	5	3
77	6	4
86	8	5
95	11	6
104	14	8
113	18	10
122	23	12

Unsymmetrical: A colorless, refractive liquid; b.p. 129°-130°C; $d_{4°}^{20°}$ 1.588; v.p. 14 mm Hg at 25°C; soluble in water to 0.02 parts : 100 parts at 20°C; miscible with alcohol, ether.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Distinctly more toxic to dogs and rabbits than chloroform. 195
      (1) Toxicity varies with animal species, solvent, route of administration and concentration in solvent.
      (2) Dilute solutions (in propylene glycol), intravenous, proved more toxic to rabbits than the pure substance or more concentrated solutions supposedly because of more rapid absorption. 1413
      (3) Fatalities in dogs, after intragastric administration of lethal doses, showed the immediate cause of death to be respiratory failure. 3378
   b) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rabbit	sc	MLD	500	Death in 24 hrs; chloroform MLD = 900 mg/k.	195
Rabbit	iv	LD_{50}	50 mm^3/k	Injected as the pure substance.	1413
Rabbit	iv	LD_{50}	26 mm^3/k	Injected as 32% solution in propylene glycol.	1413
Rabbit	iv	LD_{50}	15.4 mm^3/k	Injected as 16% solution in propylene glycol.	1413
Rabbit	iv	LD_{50}	12.5 mm^3/k	Injected as 8% solution in propylene glycol.	1413
Rabbit	iv	LD_{50}	80	Rapid injection.	1413
Dog	or	MLD	700	Chloroform MLD = 2250 mg/k.	195

b) Quantitative: (continued)

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Dog	iv	MLD	60	Death in 30 minutes; chloroform MLD = 90 mg/k.	195
Mouse	inh	MLC	40 mg/l;5850 ppm	Death in 2 hr. exposure.	1938
Mouse	inh	LC	30 mg/l;4000 ppm	Continuous exposure, death within 115 min.	1963
Dog	Intragastric	LD	0.3 cc/k	Death in respiratory failure.	3378

c) Repeated exposure, sub-acute exposure, etc.:

(1) Repeated exposure Cats, Rabbits: At 1-2 mg/liter air, 6-7 hrs./day, on 18 days of a 28 day period, induced no toxic or overt effects save drowsiness after exposure. 1961

(2) Exposure of human beings: 1963

At 0.02 mg/l, 3 ppm, noticeable by odor.
At 0.09 mg/l, 13 ppm, tolerable, without ill effects, for 10 minutes.
At 1.0 mg/l, 146 ppm, 30 minutes inhalation caused irritation of mucous membranes, sense of pressure in head, vertigo, fatigue.
At 2.3 mg/l, 335 ppm, 10 minutes inhalation, effects same as at 1.0 mg/l 30 minutes.

(3) Reported human poisonings, fatal and non-fatal, described and discussed in the following: Refs.: 1275, 1740, 1838, 2786, 993, 1068, 2757, 2059, 2401, 3402, 3396, 1965, 1066, 1303, 627, 2455, 3305, 3329.

d) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:

(1) Tetrachloroethane acts as a narcotic and CNS depressant. More effective than chloroform in inducing 2315
narcosis in animals; minimal narcotic concentration for mice at 2 hr. exposures = 10-15 mg/l, com- 1963
pared to 20 mg/l for chloroform. 1938

(2) 0.002 moles/liter arrested the isolated frog heart (chloroform 0.007 mole/liter). Another report 1071
states 0.002989 (chloroform 0.0224) mole/liter. 1789

(3) Peripheral vasodilation in mice during narcosis and lung hemorrhages in dogs have been observed. 2315,3046

(4) Pathology:

(a) Repeated exposures, mice: Lesions of parenchymatous tissue; cytoplasmic degeneration, disappearance of mitochondria; nuclear changes with chromatin pycnosis. Lesions reversible after end of exposure. 994

(b) Oral administration: Gastrointestinal irritation, hyperaemia. 994

(c) All routes: Fatty degeneration, necrosis of liver; similar, but less severe lesions in heart, 2315,3046
brain, kidney. 2212,2316,3378

(d) Corneal opacity not induced in dogs as by dichloroethane. 2965

(5) Human poisonings, symptoms, etc.:

(a) In 3 fatalities, poisoned orally: Swift unconsciousness, coma, rapid, shallow respiration, cyanosis, 1495
death in respiratory paralysis at 6, 8, 12 hrs. At autopsy: Hyperaemia of gastric mucosa, super- 933
ficial local erosions, duodenal, jejunal irritation. Lungs congested, oedematous, with subpleural 1048
haemorrhage. Brain and meninges congested. Liver and kidneys hyperaemic with some degeneration if death is delayed.

(b) Symptoms vary with degree of exposure. In light cases symptoms refer to gastro-intestinal irrita- 3199
tion, CNS disturbance: Nausea, heartburn, vomiting, gastric pain, anorexia, dizziness, headache, 1303
irritability, nervousness, insomnia. Occasionally conjunctivitis. Severe exposures intensify the preceding signs with diarrhoea, weight loss, constipation, liver enlargement and tenderness, more or less severe jaundice, exaggerated reflexes, anesthesias, paresthesias, some nerve paralysis, tremors of hand and eyelids; myelomalacia has been noted as well as nephritis with albumen and casts; when the liver is affected, bile pigments, urobilin and urobilinogen appear in urine. In very severe and fatal cases the gastrointestinal irritation is at maximum; duodenal ulcer may develop, severe jaundice with high icteric index, hepatomegaly with cirrhosis or yellow atrophy; kidneys seriously affected; patient often unconscious, with death in coma by respiratory paralysis after days or weeks.

(c) Autopsy, human: Hyperaemia, often oedema, haemorrhage of brain; acute heart dilation; lungs hyperaemic, often with oedema and with pleural or sub-pleural haemorrhage; gastro-intestinal haemorrhage may occur; kidneys hyperaemic with cloudy swelling, haemorrhage possible; liver shows yellow atrophy, possible haemorrhage, and, in delayed death, cirrhosis. 3199

2) Phytotoxicity:

a) In high concentrations, has been used as an herbicide, for example to control bindweed (Convolvulus). 162

b) As a soil fumigant, with action against perennial weeds and fungi (and nematodes) used at 13 cc/ft^3, 350 cc/yd^3, 46 lbs./1000 ft^2, 2000 lbs./acre foot. 1210

3) Toxicity for insects:

a) Toxicity of tetrachloroethane vs. Cimex lectularius, compared with other fumigants; exposure 5 hours at 25°C, in empty 12 l flasks: 2622

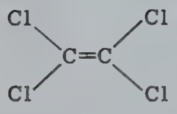
Fumigant	Approximate LC$_{95-100}$ (mg/l) For		
	Older Nymphs	Adults	Eggs
Sym.-Tetrachloroethane	35	35	25
HCN	0.4	$<$ 0.4	$<$ 0.4
Acrylonitrile	3-4	$<$ 2.5	2
Chloroacetonitrile	3-4	$<$ 3	$<$ 3

a) Toxicity of tetrachloroethane vs. Cimex lectularius, compared with other fumigants; exposure 5 hours at 25°C, in empty 12 l flasks: (continued) 2622

Fumigant	Approximate LC$_{95-100}$ (mg/l) For		
	Older Nymphs	Adults	Eggs
Chloropicrin	5-6	3	< 2.75
α,β-Dichloroethyl ether	5-6	5-6	> 6
Acrylonitrile + CCl$_4$ 1 : 1	7.5	6-7.5	6
1,1-Dichloro-1-nitroethane	8	< 8	< 8
Methyl bromide	9	< 7	< 7
Dichloroaceto nitrile	10	< 8	< 8
Trichloroaceto nitrile	11	8	< 8
Ethylene oxide	14	6-10	< 2
Methylallyl chloride	25-30	< 25	< 25
Ethyl formate	30	25-30	< 25
Ethylene oxide + ethylene dichloride 1 : 3	35	25-30	< 25
Carbon disulfide	37.5	< 30	30
Ethylene dichloride	> 50	> 50	> 50
Ethylene dichloride + CCl$_4$ 3 : 1	> 50	> 50	> 50
CCl$_4$	> 50	> 50	> 50
Trichloroethylene	> 50	> 50	> 50

177

TETRACHLOROETHYLENE (Carbon dichloride; Perchloroethylene; Ethylene tetrachloride; Didakene; Tetralex; Perawin.)



Molecular weight: 165.85

GENERAL

[Refs.: 2815, 156, 2816, 2452, 1337, 1338, 2925, 1775, 2083, 1118, 1392, 987, 1113, 3377, 2086, 851, 1801]

An insecticidal fumigant which has been tested against stored products insects. The insecticidal properties of the ethylene series increase with increased chlorination, thus the LC$_{99}$ values of sym.-dichloroethylene, trichloroethylene, tetrachloroethylene vs. Tribolium confusum, in 5 hour exposures at 25°C, empty space fumigation are, respectively, 303, 268, 99 mg/l. However, it cannot be contended that tetrachloroethylene is a particularly impressive fumigant. It is a potent anthelmintic, effective principally against hook worms, for example Ancylostoma duodenale and Necator americanus of man, with some action vs. Enterobius vermicularis. Of little value against Ascaris or ascarids. Insecticidally it has been tested in combination with ethylene dichloride. Effective vs. Fasciolopsis buski (Trematoda) in man.

PHYSICAL, CHEMICAL

A colorless liquid of ethereal odor, not flammable; m.p. ca.-22°C; freezing point -22.4°C; b.p. 121.2°C; $d_{4}^{15^\circ}$ 1.631; $n_{D}^{20^\circ}$ 1.501; v.p. 18 mm Hg at 25°C; virtually insoluble in water (1 volume in 10,000 volumes), miscible with alcohol, benzene, chloroform, ether, and most organic solvents; a solvent of fats, waxes, greases; considered in comparison with other chlorine-substituted ethylenes it may be seen that boiling point increases with chlorination, thus sym.-dichloroethylene, trichloroethylene, tetrachloroethylene boiling points are, respectively 60°C, 87°C, 121°C; with chlorination the volatility drops so rapidly that in space fumigation the increase in toxicity due to increased chlorination is more than offset by the volatility decline; at warm temperatures oxidized to phosgene.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) As the drug of choice in ankylostomiasis, the adult therapeutic dose is 3 cc, and for children 0.2 cc per year of age. 851, 1221
      (1) In the absence of alcohol or lipids in the gastro-intestinal tract, very insignificant amounts of the drug are absorbed after oral intake. This may account for the low toxicity of therapeutic doses.
      (2) Used in more than 1,000,000 patients; no severe toxic manifestations are reported.

(3) Occasionally, after therapeutic use, drowsiness, headache, vertigo and nausea may be noted.

(4) Contraindicated in ascariasis.

b) Threshold concentration in air = 200 ppm. 56

c) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD	8120 (4-5 cc)	Death in 2-9 hrs.; CNS depression.	1903
Mouse	or	LD_{50}	ca.8571 (3.2 cc)	The pure drug.	885
Mouse	or	LD_{50}	10,900 (3.9 cc)	In oil solution.	885
Rabbit	or	LD	8120 (5 cc)	Death in 17-24 hrs.	1903
Rabbit	sc	MLD	2200	Death in 24 hrs.	195
Cat	or	LD	6496 (4 cc or >)	In olive oil; death in 6-36 hrs.	1903
Cat	or	LD	5 cc/k	In milk or water; death in 24 hrs.	2085
Mouse	or	LD_{50}	4-5 cc/k	In peanut oil or peanut + castor oils.	1845
Mouse	or	LD_{100}	6 cc/k	In peanut oil or peanut + castor oils.	1845
Dog	or	LD	6496-24,360 (4-25cc)	In oil (olive); death in 5-48 hrs.	1903
Dog	iv	MLD	85	In oil; death in 30 min; chloroform MLD = 90 mg/k.	195
Mouse	inh	LC	40 mg/l; 5900ppm	2 hr. exposure; chloroform LC = 30-40 mg/l.	1938

d) Sub-acute toxicity; multiple exposure effects, etc.:

(1) Mice at 6000 ppm, inhalation: Unconsciousness in few minutes; at 3000 ppm: Unconsciousness after several hours; 2000 ppm: No loss of consciousness. 2710

(2) Rats at 3000 ppm, inhalation: Disturbances after 12 minutes exposure; at 12,000 ppm disturbances in less than 6 minutes. 2710

(3) Rats at 2500 ppm, inhalation, exposure 7 hrs. per day: Most died before 13 exposures (in 18 days) were completed. 2710

(4) Rabbits at 2500 ppm, inhalation, exposure 7 hrs. per day: 28 exposures (in 39 days) were tolerated. 2710

(5) Foxes, cattle, horses, sheep showed little injury after therapeutic doses; cattle are more susceptible than cats and other carnivores; sheep are less sensitive than cattle but more susceptible than chickens or carnivores. 2761

(6) Cats receiving 0.5 cc/k in milk or water: No toxic effects; at 1.0 cc/k: Giddiness, drowsiness, unsteadiness of hind limbs with recovery in 3 days; at 4.5 cc/k: Similar but more severe symptoms. 2085

(7) Therapeutic doses in man; side and adverse effects: 529,1775

(a) Giddiness, dizziness, vertigo in some; sense of drunkeness, occasionally vomiting, nausea, headache; rarely unconsciousness, coma with faint pulse, cold sweat; eyelid twitching (in some cases). Symptoms ordinarily clear in a short time, but in highly emaciated persons circulatory collapse and death have been noted. 2083 3377 987 2734

(8) Inhalation of tetrachloroethylene by man:

(a) At 2000 ppm slight narcosis in 5 min. At 930-1185 ppm irritation of eyes throat, marked dizziness after 2 min. At 1000 ppm slight drunkeness, no narcosis after 95 min. At 513-690 ppm after 10 min. eye, throat, nose irritation, dizziness, oral numbness, loss inhibition, some incoordination; recovery in 1 hr. At 500 ppm slight discomfort in 2 hrs. At 206-356 ppm 2 hr. exposure headache, eye burning, sinus congestion, tongue thick, impaired coordination, nausea; recovery in 1 hr. At 206-235 ppm, after 20-30 min., eye irritation, sinus congestion, nasal discharge, sleepiness, dizziness; recovery in 1 hr.; At 106 ppm not objectionable, no distinct effects; at 50 ppm recognizable by odor. 2710 477

2) Pharmacological, pharmacodynamical, physiological, etc.; higher animals:

a) Absorption; Fate:

(1) Absorbed by inhalation via lung. Not absorbed (in absence of fats) from gastro-intestinal tract in dogs, but absorbed in sufficient amounts to yield narcosis in mice, rabbits, cats, young puppies. Alcohol facilitates absorption. 1903

(2) Moderate dermal uptake (mice). 2788,1493

(3) Metabolic fate unknown; in urine an unidentified water-soluble, ether-insoluble material appeared after exposure. Partial excretion via lung. 193

b) Nerve system effects:

(1) Minimal narcotic concentration (mice) = 20 mg/l (2950 ppm) compared with 20 mg/l for chloroform, 25 mg/l for trichloroethylene. 1938

(2) 67 mg/l (9900 ppm) gave anesthesia of dog with narrow safety margin. 1903

(3) In cats marked irritation, salivation, sneezing, convulsions upon anesthesia. 1903,1963

Narcotic action in mice 641

mg/l	ppm	Equilibrium Disturbance In (minutes)	Resting In (minutes)	Remarks
16	2400	64	135	No narcosis 160 minutes.
17	2500	42	67	No narcosis 120 minutes.
18	2600	17	30	Narcosis 47 min.; recovery after 150 min.
23	3400	11	33	Narcosis 54 min.; 1/3 dead 180 minutes after exp.
25	3700	12	21	Narcosis 31 min.; 2/3 dead 164 minutes after exp.
40	5900	4	8	Narcosis 14 min.; 100% dead 49 minutes after exp.

c) Other effects:
   (1) Excess by inhalation or subcutaneous routes: Fall in blood pressure, not prevented by vagal section or atropine. 1903
   (2) Depression of heart and circulation. 544
   (3) Effects resembling CCl_4, on the circulation. 2397

d) Pathology:
   (1) No pathology in dogs at 0.7 cc/k/19 consecutive days or inhalation of 14,600 ppm in air for 24 days. 1702
   (2) Rats at 7000 ppm 8 hrs./day/to 1200 hrs. exposure: No effect on fertility; congestion with cloudy granular swelling of liver, no fatty degeneration. 477
   (3) Adult dog: No liver lesions; puppies, cats: Fatty changes without necrosis or functional change. 1903
   (4) Dogs after 0.2 cc/k, sans purgation: Degeneration and atrophy of hepatic cells involving most of lobules. Fatty infiltration after single and repeated doses. 1338, 544
   (5) Liver damage in various animals. Rats after repeated exposures 7 hrs./day showed cloudy swelling of liver with few fat vacuoles; rabbits: Slight degeneration centrally in lobules; Guinea pigs exposed 169 times in 236 days at 7 hrs./day to 400 ppm: Fatty degeneration and slight cirrhosis of liver. 2761,2710
   (6) Kidney effects after prolonged exposure (rat): Congestion, cloudy swelling, increased secretion in tubules, desquamation. In cats: glomerular congestion, cytological changes in tubule epithelium Others report no effects on kidney. 2761, 477 2085,1903
   (7) Gastro-intestinal effects: After single and repeated doses: Shriveled and spongy condition of small intestine; severe inflammation. 544
   (8) Cardiac effects; in dogs: Fatty infiltration of myocardium. 544

e) Not a successful narcotic for human anaesthesia. 1047

3) Toxicity for insects:

a) Induces severe narcosis in Tribolium confusum which, followed by recovery, does not impair reproduction nor reproductive organs in ♀♀. 2452

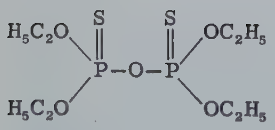
b) Vs. Tribolium confusum, at 25°C, 5 hour exposure, empty flask fumigation: 156,2816

Substance	LC_{50} (mg/l)	LC_{99} (mg/l)
Tetrachloroethylene	55	99
Trichloroethylene	108	268
Sym-Dichloroethylene	154	303

   (1) Tribolium confusum exposed at 25°C, 760 mm Hg in the presence of wheat flour as absorbent: LC_{50} = 440 mg/l as compared to 54 mg/l in similar exposures in absence of absorbent. 1013
   (2) Sorption in wheat flour (patent flour) after 5 hrs. exposure at 25°C to a concentration of 200 mg/l = 113.7 mg, sorption ratio (CS_2 = 1) = 10.4; in exposures of 3 inches of flour to 200 mg/l concentrations for 24 hrs., 57.6 mg passed through the layer of flour. 3013

178

TETRAETHYL DITHIONOPYROPHOSPHATE (Tetraethyl dithiopyrophosphate; Sulfatep; Sulfotepp; Dithione; ASP 47; E-393; Bladafume)



Molecular weight: 322.25

GENERAL (Also consult TEPP, HETP, NPD) [Refs.: 353, 2231, 129, 2120, 2773, 2244, 2769, 326, 2867, 1690, 554, 2118, 3106]

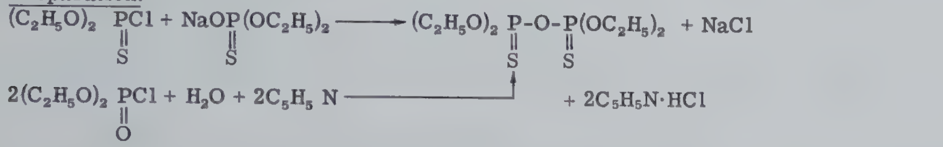
An insecticide of high contact toxicity for a wide variety of insects which belongs to that general class of contemporary insecticides commonly referred to as organic phosphates, or "organophosphorus" insecticides. Essentially, this compound is the dithio-(= dithiono-) analogue of tetraethyl pyrophosphate, TEPP, q.v., which accounts for the designation "Sulfatep" or "Sulfotepp." The substitution of two sulfur atoms for two oxygen atoms on the phosphorus atoms does not materially reduce the insecticidal potency, but does materially reduce the toxicity to mammalian animals. TEPP is ca. 10 times more toxic for the mouse, intraperitoneally, than Sulfatep, the dithio-analogue. TEPP is ca. 4 times as toxic as Sulfatep for Apis mellifera and 5 times as toxic for aphids. However, the toxicity of TEPP for insects being so great, even this decline leaves plenty of potency to spare for Sulfatep. Sulfatep, although highly toxic by contact for insects, has a comparatively poor persistence on sprayed foliage, probably because of a high volatility. A potent inhibitor of mammalian choline esterase(s) in vivo and in vitro. A powerful acaricide, giving higher kills of adult, resistant Tetranychus bimaculatus than any organic phosphate used as a fumigant aerosol; even more effective against the young active stages, although frequent applications are needed to keep the resistant biotypes in check. Potently effective as an insecticidal "smoke" for greenhouse use.

PHYSICAL, CHEMICAL [Refs.: 1339, 2773, 3106, 129, 2120, 2769]

Pure: A pale, yellow liquid; b.p. 136°-139°C at 2 mm Hg, 110°-117°C at 0.2 mm Hg; $d^{25°}$ 1.196; $n_D^{25°}$ 1.4578; v.p. 0.1 mm Hg at 92°; soluble in water at room temperatures to ca. 0.0025%, 1 part : 1500 parts, 25 mg/liter; soluble in alcohols, ethers, esters, ketones, aromatic hydrocarbons, methylchloride; relatively insoluble in kerosene, aliphatic oils; sulfur-like odor; highly volatile; slowly hydrolyzes in aqueous solution. The technical product, ca. 90% pure, is a dark to brown liquid; b.p. 131°-135° at 2 mm Hg; $n_D^{25°}$ 1.4725; stable in lime water.

a) Formulations: As aerosols (not recommended for livestock, household, or industrial use); as Bladafume for use in "smoke" generators.

b) Preparation:



$$(C_2H_5O)_2\underset{\overset{\|}{S}}{PCl} + NaO\underset{\overset{\|}{S}}{P}(OC_2H_5)_2 \longrightarrow (C_2H_5O)_2\underset{\overset{\|}{S}}{P}\text{-}O\text{-}\underset{\overset{\|}{S}}{P}(OC_2H_5)_2 + NaCl$$

$$2(C_2H_5O)_2\underset{\overset{\|}{O}}{PCl} + H_2O + 2C_5H_5\,N \longrightarrow \quad + 2C_5H_5N\cdot HCl$$

TOXICOLOGICAL (Also consult the general treatment Organic Phosphates.)

1) Toxicity for higher animals:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	sc	LD	8		2773
Rat	or	LD_{50}	5	TEPP LD_{50} or = 1.2-2 mg/k; NPD* 1450 mg/k.	2231,3106

*=Tetra-n-propyl dithionopyrophosphate.

2) Chronic effects, long term administration:

a) Rats, fed Sulfatep in diet for 1 year at 60 ppm: No gross effects; at 180 ppm: No tissue damage. 1953

3) Residue hazard:

a) Apparently not great. On lettuce at an initial magnitude of 25 ppm only a trace was detectable after 14 days, the half-life being 1 day; on tomato foliage at an initial magnitude of 10 ppm only a trace was detectable at 14 days with a half-life of 2 days. 2877, 129

4) Phytotoxicity:

a) Tested, without plant injury, on 140 species of greenhouse plants. 1690

(1) Injury noted to papaya plants, carnation flowers, orchids of the genus Cattleya; injury may be avoided by airing the greenhouse at 2.5-3 hours after beginning the application of Sulfatep as a "smoke."

5) Toxicity to insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Anopheles quadrimaculatus (larva)	Medium	MLC_{100}	0.0025 ppm	0.001 ppm yielded 74% kill.	2020
Apis mellifera (adult)	Topical	LD_{50}	5.0 ug/g	Para-oxon = 0.6; methyl parathion = 1.7; NPD = 200; TEPP = 1.2; parathion = 1.7; EPN® = 3.0; DFP = 30.	2231
Musca domestica (adult)	Topical	LD_{50}	5.0 ug/g	NPD = 15; TEPP -?; parathion = 0.9; para-oxon = 0.5; EPN® = 1.9; methyl parathion = 1.0; chlorthion® = 16.5; malathion = 28; diazinon = 4.6; DFP = 15.	2231

(1) Used as an insecticidal "smoke" in greenhouses (in general, 4 applications at 3-4 day intervals for scale, mites, mealy bugs; 1 application for aphids, with generators containing 15% Sulfatep) effective vs. Pseudococcus citri, P. adonidum, P. martimus, Phenococcus gossypii, Aonidiella aurantii, Hemiberlesia lataniae, Pinnaspis aspidistrae, Coccus hesperidum, Saissetia hemisphaerica, S. oleae, Tetranychus bimaculatus, Aceria paradianthi, Hemitarsonemus latus and various aphid species. Ineffective vs. Tarsonemus pallidus and Tetranychus bimaculatus (resistant biotype). 1690

(2) Comparative toxicity of Sulfatep and other compounds, vs. Anopheles quadrimaculatus 4th instar larvae in laboratory tests; insecticides applied as acetone-water suspensions: 1766

Compound	% Mortality 48 hrs. At							
	0.1	0.05	0.025	0.01	0.005	0.0025	0.001	0.0005
	(ppm)							
Sulfatep	100						74	34
Parathion	100					96	56	34
EPN®	100					96	32	—
Methylparathion	100					67	—	—
O,O-Dimethyl O-(2-chloro-4-nitrophenyl) thiophosphate	100			96	86	62	62	44
Malathion	100		96	80	80	60	40	24

(2) Comparative toxicity of Sulfatep and other compounds, vs. Anopheles quadrimaculatus 4th instar larvae in laboratory tests; insecticides applied as acetone-water suspensions: (continued) 1766

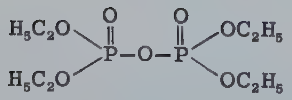
Compound	% Mortality 48 hrs. At (ppm) 0.1	0.05	0.025	0.01	0.005	0.0025	0.001	0.0005
Ethyl O-nitrophenyl thionobenzene phosphonate	100 ————				70	80	4	—
Diazinon	100 ————				36	20	—	—
Para-oxon	100 ————			82	50	—	—	—
O,O-Dimethyl O-(3-chloro-4-methylumbelliferone) thiophosphate	100 ————			64	46	24	—	—
Chlorthion®	100 ———		88	76	44	—	—	—
Potasan®	100	98	56	30	5	—	—	—
O,O-Diethyl O-piperonyl thiophosphate	100	94	58	26	—	—	—	—
NPD	94	—	62	30	—	—	—	—
DDT	—	—	—	100	94	49	24	—

(3) Field experiences with Sulfatep and other insecticides vs. Anopheles quadrimaculatus and Anopheles crucians: 1766

Compound	% Mortality 24 Hrs. At Lbs./Acre Shown (ppm) 0.25	0.1	0.05	0.025	0.01	0.005	0.0025	0.001
Sulfatep	—	85	72	73	63	53	30	—
EPN®	—	—	95	96	96	95	92	91
O,O-Dimethyl O-(3-chloro-4-methylumbelliferone) thiophosphate	—	—	98	98	99	96	91	84
Parathion	—	—	97	97	92	99	88	—
Methyl parathion	—	100	98	83	69	51	50	—
Ethyl O-nitrophenyl thionobenzene phosphonate	—	99	80	88	75	70	69	71
Chlorthion®	100	99	82	73	57	50	—	—
Diazinon	—	97	97	79	58	65	55	53
O,O-Dimethyl O-(2-chloro-4-nitrophenyl) thiophosphate	—	99	72	78	49	30	—	—
NPD	100	97	84	87	79	—	—	—
Para-oxon	—	90	77	54	46	45	49	31
Malathion	90	78	79	68	60	—	—	—
O,O-Diethyl O-piperonyl thiophosphate	—	—	78	64	75	74	45	35
Potasan®	—	77	59	72	52	—	—	—
DDT	—	—	99	98	99	98	95	92

179

TETRAETHYL PYROPHOSPHATE (TEPP; TEP; Bladan; Bladex; Nifos; Nifos T; Vapotone; Fosvex; Hexamite; Tetron etc.)



Molecular weight: 290.2

GENERAL (Also consult HETP, Sulfatep, NPD, Organic Phosphates, Miticides and Acaricides)
[Refs.: 353, 2231, 2120, 129, 89, 713, 314, 1407, 2769, 2773, 2775, 2427, 594, 1057, 1458, 2577, 1341, 2699, 2701, 2702, 2043, 1458, 852, 2815, 1059, 757, 3104, 2081, 1284, 1801, 1221, 1169, 750, 864, 134, 724, 392, 326, 436, 2878]

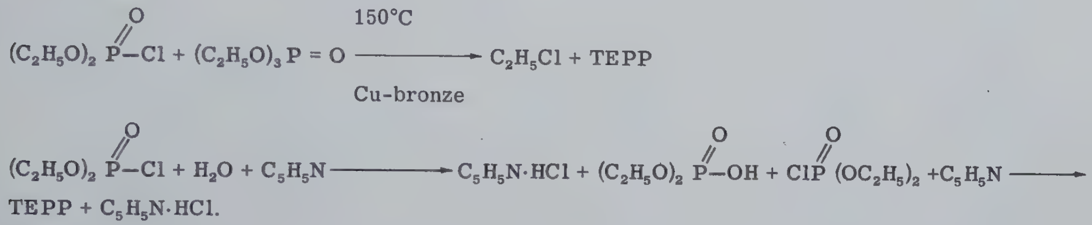
One of the most widely tested and used of that modern class of insecticides commonly termed organic phosphates, or "organophosphorus" insecticides. A powerful contact acaricide and insecticide, particularly vs. aphids, but with virtually no residual activity because of rapid hydrolysis in aqueous solution or in the presence of moisture. An intensely poisonous and hazardous substance for man and mammals, as well as vertebrates in general. Potently inhibits choline esterase(s) in vivo and in vitro, entering into a combination with the esterase which is partially reversible in vivo. Stable, when protected from air and moisture, TEPP may be kept for months in peanut oil or propylene glycol solution. At the beginning of its insecticidal use, TEPP was confused with HETP, then prepared as a mixture of esters, of which TEPP was later found to be the principal and by far the most active component. Hazardous in handling, manufacture, formulation and application, TEPP calls for all adequate precautions. These being met, TEPP is an extremely useful insecticide in the control of "soft-bodies" insects, red spiders and diverse other acarines. The toxic action is powerfully cholinergic.

PHYSICAL, CHEMICAL

Pure: A colorless, mobile, hygroscopic liquid which may have a faintly aromatic smell; b.p. 104°-110°C at 0.08 mm Hg, ca. 100°C at 0.01 mm Hg, 150°C at 10 mm Hg, 125°C at 0.1 mm Hg decomposing at higher temperatures than the boiling point, 135°-138° at 1 mm Hg; $d_{25°}^{25°}$ 1.19, $d_{25°}$ 1.1810, $d_0^{20°}$ 1.1847, $d^{24°}$ 1.1901; $n_D^{25°}$ 1.4170-1.4180; volatile; decomposes at 170°C; miscible with water in all proportions; soluble in acetone, alcohol, benzene, carbon tetrachloride, chloroform, diacetone, ethyl acetate, glycerine, o-dichlorobenzene, pine oil, toluene, xylene, alkyl naphthalenes; insoluble in kerosene, petroleum oils; corrosive to metals; hydrolyzes rapidly in water and aqueous solutions, must be used promptly; at 25°C hydrolysis is 50% complete in ca. 7 hours, at 38°C in 3.3 hours, at 25°C hydrolysis is ca. 99% complete in 45.2 hours and at 38°C in 22 hours; the hydrolysis rate constants are at 25°C 1.7×10^{-3} min.$^{-1}$, at 38°C 3.5×10^{-3} min.$^{-1}$ ($K = 160\,[OH^-] + 1.6 \times 10^{-3}$ min.$^{-1}$); hydrolysis leads to non-toxic substances; heating of the pure substance to 208°-213°C yields ethylene and metaphosphoric acid; crude products (catalyzed by impurities) undergo this decomposition at 140°C and above. The crude product is an amber liquid, of specific gravity ca. 1.2 at 25°C which is distillable under vacuum to yield the pure form.

a) Formulations: Aerosols 5%, 10% (for greenhouse use only); dusts 0.66—1%, 1-1.2%; sprays 10%, 16%, 20% 35%, 40%. Incompatible with alkalis, calcium arsenate, Paris green, lime, lime-sulfur, lime and Bordeaux Mixture; compatibility questioned with lead arsenate, cryolite, rotenone, pyrethrum, nicotine, dithiocarbamates, dinitro-compounds.

b) Preparation:



$$(C_2H_5O)_2\overset{O}{\overset{/\!/}{P}}-Cl + (C_2H_5O)_3P=O \xrightarrow[\text{Cu-bronze}]{150°C} C_2H_5Cl + TEPP$$

$$(C_2H_5O)_2\overset{O}{\overset{/\!/}{P}}-Cl + H_2O + C_5H_5N \longrightarrow C_5H_5N\cdot HCl + (C_2H_5O)_2\overset{O}{\overset{/\!/}{P}}-OH + Cl\overset{O}{\overset{/\!/}{P}}(OC_2H_5)_2 + C_5H_5N \longrightarrow TEPP + C_5H_5N\cdot HCl.$$

TOXICOLOGICAL

1) Acute toxicity for higher animals:

a) A potent poison for mammals; rapidly absorbed, with an intense toxicity by oral, dermal and inhalation routes. 89, 353, 852, 1458, 851, 1221

(1) For animals in general: LD_{50} oral = 50 mg/k or less (single dose), LC_{50}, inhalation = 200 ppm, exposure 1 hour, LD_{50}, cutaneous = 200 mg/k, 24 hour contact. 1407

b) Dangerous acute dose, man: Experiences gained from testing of TEPP therapeutically in myasthenia gravis: Single dose of 5 mg or 3.6 mg daily for 2 days or 2.4 mg/day for 3 days parenterally, or 7.2 mg every 3 hours, orally, for 3-5 doses produced symptoms in normal subjects as did slightly larger doses in myasthenia gravis patients under atropine premunition. 89

(1) Initial treatment dose in myasthenia = 10 mg, oral, in propylene glycol or 2.5 mg, intramuscular, in peanut oil or water. The initial dosage exerts little effect on muscle strength; repetition in 6-24 hrs. slightly increases muscle strength; 3rd dose, 1 hr. later, yields good remission of muscle weakness. Atropine aborts the muscarinic, but not the nicotinic, side-effects. 1284

(2) In continued daily use, the cumulative effect on choline esterase is marked; the margin of safety is narrow. 851

(3) Topical application in glaucoma: Administered at 0.05-1.0% in peanut oil. Presents no advantages over DFP (di-isopropyl fluorophosphate); tends to sensitize the conjunctiva; induces ciliary spasm, myopia, headache. 1221, 851

(4) At the dosages used in myasthenia gravis (vide supra), symptoms came suddenly 30 minutes after final dose, being: Local fasciculations, anorexia, nausea, sweating, salivation, abdominal cramps, giddiness, restlessness, insomnia, paraesthesia, unusual dreaming. 89, 1284

c) Estimated doses for severe symptoms, man: 5 mg, intramuscular; 25 mg, oral. (5 mg dose/man = ca. 0.07 mg/k) 1281

d) Estimated lethal doses, man: 20 mg, intramuscular; 100 mg, oral. 1281, 852

e) Inhibition of choline esterase, man; in vitro: 1284, 326

*ID_{50}, serum ChE = 8.6×10^{-10}M 861, 859
ID_{50}, plasma ChE = 5×10^{-9}M
ID_{50}, erythrocyte ChE = 3.5×10^{-8} M
ID_{50}, brain ChE = 3.2×10^{-8} M
ID_{50}, brain ChE (Rat) = 4×10^{-9} M; (Mouse) 4×10^{-9}

* = Concentration to produce 50% inhibition of choline esterase or Inhibition Dose 50%.

f) LD_{50} and ID_{50} in vitro, Mouse; TEPP and related compounds: 861

Compound	LD_{50}, ip (mg/k)	ID_{50}, ChE, In Vitro
Tetramethyl pyrophosphate	1.7	1.8×10^{-8} M
TEPP	0.85	4.0×10^{-9} M
Dimethyl diethyl pyrophosphate	1.1	8.0×10^{-9} M
Dimethyl diisopropyl pyrophosphate	2.5	2.0×10^{-7} M
Tetraisopropyl pyrophosphate	16.0	1.4×10^{-6} M

(1) Relation (Rat) of LD_{50} subcutaneous, oral, percutaneous = 1 : 2.5 : 3.5, (TEPP). 89

g) Hazard for man: Very toxic on acute exposure. Physical and chemical properties are such that hazard results from abuse or carelessness. Extreme instability reduces hazard to the public from residues on food plants, crops, fruits, etc. 1458

(1) Fatal accidents have all (reportedly) involved suicide or gross carelessness (such as spills on skin or 89
clothing of the TEPP concentrates). Non-fatal accidents have been reported among agricultural workers 129
and airplane pilot applicators. A single drop in the eye is probably fatal.

h) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	7.0 ± 0.3		1057
Mouse	sc	LD	1.0		2769
Mouse	sc	LD_{50}	0.9		89
Mouse	ip	LD	0.85		2081
Mouse	ip	LD_{50}	0.82		3104,3105
Rat	or	LD	1.24		808
Rat	or	LD_{50}	1.2-2.0		2231
Rat ♀	or	LD_{50}	1.2 ± 0.1		1057
Rat ♂	or	LD_{50}	2.0 ± 0.15		1057
Rat	or	LD_{50} ca.	1.2		1951
Rat	or	LD_{50}	ca.1.4		2081
Rat	sc	LD_{50}	0.7		89
Rat	ip	LD_{50}	0.65		2081
Rat	inh	LD_{50}	0.8-1.0		129
Guinea Pig	or	LD_{50}	2.3 ± 0.19		1057
Rabbit	ct	LD_{50}	5	Single acute exposure; technical TEPP.	2231
Rabbit	ct	LD_{50}	2.0-2.5		89
Rabbit	ct	MLD	0.04 cc/k		744,1407
Rabbit	ct	Toxic	48		2120
Cat	sc	LD_{50}	2.5-3.0		89
Cattle	Spray, Dip	Min.Toxic Conc.	$>$ 0.06%	Single spray or dip; emulsion or suspension.	202
Cattle	Spray, Dip	Min.Toxic Conc.	$<$ 0.03%	Single spray or dip; emulsion or suspension.	2570
Fish	Medium	LC	0.25 ppm or more	Parathion (Threshold Conc., Bluegill) = 0.2 ppm.	2026

N.B. Species and sex differences in susceptibility are not marked. 852

2) Chronic toxicity, higher animals:

a) Exposure to any organic phosphate insecticide lowers the choline esterase level; until the enzyme is regenerated to normal levels the exposed organism remains susceptible to relatively small doses of TEPP. Small doses at frequent intervals are largely additive in effect. 89

(1) Stated to present little or no chronic hazard because its rapid hydrolysis leaves no toxic residue. Hy- 2231
drolytic products not toxic. The hydrolytic product, diethyl o-phosphoric acid, fed (Rat) at 5000 ppm 852
for 20 weeks was without effect. 20% TEPP fed (Rat) at 1000 ppm for 12 weeks: No gross effects. 353

(2) Stated to be rapidly destroyed and not to be stored in the animal body. 129

(3) Nonetheless, repeated exposures sufficient to influence choline esterase levels downward must be con- 852
sidered hazardous. A balance must be considered between frequency of exposure, rate of ChE inhibi- 851
tion, and ChE regeneration. Also to be considered is the reversibility of the TEPP—ChE complex *in vivo*.

b) Precautiouns should be followed explicitly, as should directions; protective clothing, respirators, gloves essential; no eating or smoking during handling, formulation or application are all de rigueur. 129

c) Residues on crops: No removal methods necessary (if directions are followed as to time between application and harvest) since decomposition is rapid; no soil accumulation.

d) To be kept in mind is the ready absorption of TEPP by the skin with only a slight sense of irritation. The 1949
danger level for repeated inunction is reported as 5 mg/k. 353

(1) 6-8 times as toxic as HETP; commercial TEPP (40%) is 3 times as toxic as commercial HETP with a 10-20% TEPP content.

(2) Rapid decrease in toxicity in presence of water; toxicity declines at same rate as hydrolysis procedes. A 1% solution in water becomes, in 24 hours, less than 1/10th as toxic as the fresh solution, and at 3 days ca. 1/1500th as toxic. 1407

3) Pharmacological, pharmacodynamic, physiological, etc.; higher animals: [Refs.: 392, 1543, 589, 724, 1710, 1851, 2728, 3180, 3314]

a) Also consult the general treatment titled Organic Phosphates.

b) The fundamental mechanism of toxic and pharmacodynamic action is the inhibition of the enzyme(s) choline 89,851
esterase(s). This leads to the accumulation of acetylcholine with the attendant signs of cholinergic 2699,1221
intoxication. 713, 326

(1) Evokes marked muscarinic, nicotinic and CNS effects. 392,1278

(2) The chemical basis for the affinity of TEPP-ChE is postulated as follows: The phosphorus 1284,1281,852
atom represents a strong electrophilic center reactive with the esteratic group of ChE like the electrophilic carbonyl-carbon atom of acetylcholine. The resulting complex is highly stable, and *in vitro* has the characteristics of irreversible ChE inhibition, although the recovery of rabbits, poisoned

with TEPP (rapid as compared with diisopropyl fluorophosphate poisoning of like intensity) suggests some in vivo reversibility.

c) The onset of effects is more rapid with TEPP than with DFP. Moreover, the effects in non-fatal intoxication are more transient.
   (1) TEPP being more water soluble than DFP, the nicotinic effects are more pronounced; generalized muscle fasciculations are prominent and quickly developed.
   (2) The muscarinic effects in man and animals include: Nausea, vomiting, cardiospasm, stimulation of sweat, salivary, tear glands; also: Bronchoconstriction, miosis, urinary frequency, bradycardia, cramps, diarrhoea.
   (3) CNS effects (less prominent than with DFP): Giddiness, blurred vision, convulsions, drowsiness, strange dreaming, loss of sensitivity to light, loss of depth perception (important to airplane spray pilots!), coma and depression follow initial stimulation.
   (4) There may be pulmonary oedema and cyanosis. Respiratory arrest, due to paralysis of skeletal myoneural junctions and of the medullary respiratory center, ends in death.
   (5) The stimulant effect of TEPP on the intestine is less than with DFP (non-specific choline esterase(s) prevails in the intestinal muscularis).

d) Laboratory examination confirms the lowering of choline esterase levels in poisoned animals. The electrocardiogram reveals marked changes. Readily hydrolyzed by liver enzymes to inactive phosphoric acid derivatives.

e) Atropine provides both premunition and antidote for the muscarinic, but not for the nicotinic effects. The patient must be kept fully "atropinized" (1-2 mg/hour up to an intake of 10-20 mg in a day) particularly to control respiratory symptoms.
   (1) Morphine, theophylline, aminophylline are contraindicated!!
   (2) Atropine does not protect against muscle weakness. Oxygen is useful. Need for artificial respiration may be sudden.
   (3) The acute emergency endures 24-48 hours during which constant watch of patient must be maintained. Favorable response to atropine (1-2 doses) does not guard against sudden and fatal relapse. Medication must continue through the entire period of emergency.

f) Following any exposure productive of symptoms, all further exposure to organic phosphates must be avoided. Sensitivity endures until choline esterase restoration is complete.

4) Hazard to wildlife:
   a) Indubitably hazardous under suitable conditions of exposure. Consult the table of toxicity for higher animals.

5) Phytotoxicity:
   a) Phytotoxic hazard considered low; damage noted on certain tomato and Chrysanthemum varieties. 129
      (1) At concentration of 1 : 1000 (a concentration stronger than required to control aphids or mites) no damage noted to: Asparagus sprengeri plumosa, broccoli, cauliflower, Chrysanthemum, fern, cucumber, egg plant, peas, Poinsettia, roses, Antirrhinum, soy-bean, string-bean, slight burn to tomato foliage. 1407
      (2) Tomatoes and Chrysanthemum alone of 130 species tested, showed foliage injury from 10% aerosols at 10 g/1000 ft^3 with spot necrosis of leaves. Under hot, sunny conditions hazard may exist for roses and carnations. Thermal vapors have scorched foliage. Tomatoes have been killed when soil was watered with solutions of $>0.2\%$. Foliage of pear, peach and plum orchards has shown red spots with perforation; the hazard was enhanced by high temperatures and high humidity. 84,2524 2743,3399
      (3) Increased yield of potatoes (independent of insecticidal effect) is reported for treated potato plants. Nutritional effect? 3355

6) Toxicity for insects:
   a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Apis mellifera (adult)	Topical	LD$_{50}$	1.2 μg/g		2231
Apis mellifera (adult)	or	LD$_{50}$	0.75 μg/bee		910
Apis mellifera (adult)	or	LD$_{20}$24 hr.	0.052 μg/bee		1718
Apis mellifera (adult)	or	LD$_{50}$24 hr.	0.065 μg/bee		1718
Apis mellifera (adult)	or	LD$_{90}$24 hr.	0.093 μg/bee		1718
Apis mellifera (adult)	Contact Spray	LDeposit$_{20}$	35.8 mg/cm^2×10^{-5}		1718
Apis mellifera (adult)	Contact Spray	LDeposit$_{50}$	44.5 mg/cm^2×10^{-5}		1718
Apis mellifera (adult)	Contact Spray	LDeposit$_{90}$	62.1 mg/cm^2×10^{-5}		1718
Anopheles quadrimaculatus (larva)	Medium	MLC$_{100}$ 24 hrs.	10 ppm	42% mortality at 1.0 ppm.	2020
Blattella germanica (adult) ♂	Dipping	LC$_{50}$	0.0575 cc/l	Non-Chlordane R biotype.	1259
Blattella germanica (adult) ♀	Dipping	LC$_{50}$	0.153 cc/l	Non-Chlordane R biotype.	1259
Blattella germanica (adult) ♂	Dipping	LC$_{90}$	0.11 cc/l	" " " "	1259
Blattella germanica (adult) ♀	Dipping	LC$_{90}$	0.395 cc/l	" " " "	1259
Blattella germanica (adult) ♂	Dipping	LC$_{50}$	0.112 cc/l	Chlordane-R biotype order resistance 1.9.	1259
Blattella germanica (adult) ♀	Dipping	LC$_{50}$	0.265 cc/l	" " " " " 1.7.	1259
Blattella germanica (adult) ♂	Dipping	LC$_{90}$	0.165 cc/l	" " " " " 1.5.	1259
Blattella germanica (adult) ♀	Dipping	LC$_{90}$	0.512 cc/l	" " " " " 1.2.	1259
Diataraxia oleracea (larva)	or	LD$_{50}$	43 μg/larva	Larval wgt. 0.32 g; dusted leaf method.	3245
Diataraxia oleracea (larva)	or	LD$_{50}$	69 μg/larva	Larval wgt. 0.42 g; " " "	3245
Diataraxia oleracea (larva)	or	LD$_{50}$	1.12 μg/larva	Larval wgt. 0.56 g; " " "	3245
Melanoplus differentialis (adult)	Topical	LD$_{50}$	4.4 μg/g	As solution in acetone dioxane.	3267
Musca domestica (adult)	Contact Spray	LC$_{50}$ 24 hrs.	0.069 mg/cc	Knockdown in 10 min. at LC$_{50}$ = ca. 70%; turntable method.	2033
Musca domestica (adult)	Contact Spray	LC$_{50}$ 24 hrs.	0.095 mg/cc	Spray in acetone-kerosene 1 : 1. " "	1164
Myzus porosus	Contact Spray	LC$_{50}$	0.0025%		2053
Myzus porosus	Contact Spray	LC$_{50}$	1 : 40,000	$>$50% kill on roses; aqueous sol.	2053
Myzus porosus	Contact Spray	LC$_{95}$	1 : 10,000	95% kill on roses; aqueous sol.	2053
Periplaneta americana	Injection	LC$_{50}$ approx.	6.75 μg/g	Attributed to HETP, probably TEPP.	505
Tetranychus bimaculatus	Aerosol	LC$_{50}$	0.08 g/1000 ft^3	LC$_{50}$ HETP = 0.25 g/1000 ft^3.	1558

b) Comparative toxicity TEPP and other compounds vs. acarines and insects:

(1) Vs. Tetranychus bimaculatus** as aerosols, exposure 6 hrs. at 70°F ± 4°. 1558

Dose (g/1000 ft³)	% Mortality With					
	TEPP			HETP		
	24 hrs.	3 days*	7 days*	24 hrs.	3 days*	7 days*
0.063	43.7	35.8	21.6	—	—	—
0.125	61.5	39.8	38.2	41.5	31.4	33.6
.17	—	—	—	46.3	35.9	33.6
.25	68.3	59.6	42.7	55.3	49.3	36.5
.5	63.6	62.9	42.7	55.6	42.6	46.1
1.0	84.5	62.4	55.8	62.7	59.4	41.6
3.0	93.5	53.8	48.6	84.9	59.1	37.0
5.0	98.2	78	77.8	83.9	64.7	50.3
7.0	96.0	89.7	85	92.0	79.3	54.0
9.0	96.6	79.5	62.2	87.3	76.7	54.7
11.0	99.0	86.8	68.2	85.6	77.8	60.1

* Eggs and quiescent forms survived to renew infestation, unless repeated applications were made at suitable intervals.

** In certain greenhouses of several localities, biotypes of resistant T. bimaculatus have appeared and become widely disseminated; TEPP, as aerosol in methyl chloride, at concentrations which yielded 97% or more control of non-R biotypes yielded but 12% control of R-biotypes. 2867

(2) Vs. Myzus porosus on roses HETP yielded ca. 90% kills at 1 : 5000 aqueous solution; TEPP yielded 95% kills at 1 :10,000 more than 50% kills at 1 : 40,000; Nicotine at 1 : 2000 yielded 50% kills. 2701

(3) Vs. Melanoplus differentialis (adult); topical application; in acetone, dioxane: 3267

Substance	LD_{50} (μg/g)
TEPP	4.4
HETP	18.4
Parathion (tech.)	0.7; 0.8
Dieldrin	1.4
Aldrin	1.8
Heptachlor	2.6; 1.6
Lindane	1.6; 3.4
Chlordane	16.3; 9.8
Toxaphene	73.9; 61.0
DDT	9380.0; 0

(4) Vs. Musca domestica (adult) as acetone-kerosene (1 : 1) sprays, applied by the Turntable Method: 1164

Substance	Concentration (mg/cc)	Mean Kill 24 Hrs. (%)	Mean Conc. For 50% Kill 24 Hrs.	Relative Toxicity At LC_{50} (HETP=1)
TEPP	0.3	100	0.095 ± .01	5.5 ± 0.7
	.15	70		
	.074	43		
	.037	10		
HETP	.64	58	0.52 ± .05	1 (standard)
	.32	33		
	.16	3		
Parathion	.079	100	0.03 ± .003	17 ± 2
	.039	71		
	.026	47		
	.02	11		
Pyrethrins (standard mixture)	2.0	70	1.2 ± .14	0.43 ± .06
	1.0	45		

(5) Vs. Musca domestica as contact sprays, applied by a Turntable Modification of the Peet-Grady Method: 2033

Compound	Conc. (mg/cc) To Yield 50% Kill In 24 Hrs.	"Knockdown" In 10 Min. At LC_{50}
TEPP	0.069	ca. 70%
Dieldrin	.017	0
Parathion	.02	0
Methyl parathion	.025	0
Lindane	.046	0
Heptachlor	.052	0
Aldrin	.056	0
Chlordane	.25	0
DDT	.35	0
Malathion	.48	0

(5) Vs. *Musca domestica* as contact sprays, applied by a Turntable Modification of the Peet-Grady Method: 2033

Compound	Conc. (mg/cc) To Yield 50% Kill In 24 Hrs.	"Knockdown" In 10 Min. At LC_{50}
Toxaphene®	.68	0
Tetrapropyl dithionopyrophosphate	.69	0
Dilan	.72	ca. 30%
Isolan	1.15	100%
Allethrin	1.5	100%
Pyrolan	5.5	100%

(6) Vs. *Diataraxia oleracea* (larva) final instar; oral, leaf method (settling tower dusted): 3245

Substance	LD_{50} (μg/larva) At Larval Weight Of 0.32 g	0.42 g	0.56 g	Ratio Of LD_{50} For Body Wgt. Ratio Of 1 : 2
TEPP	43	69	112	1 : 3.3
Lead arsenate	66	78	91	1 : 1.5
Parathion	2.6	3.4	4.6	1 : 2
Lindane	13	26	59	1 : 6.5
DDT	4.5	12	33	1 : 11.2

(7) Vs. *Blattella germanica*, Chlordane-R and Chlordane-non-R biotypes; By dipping method. Values = concentration as cc/l for chlordane and TEPP, g/l for Lindane. 1259

Insecticide	Sex	Non-R		Chlordane-R		Order of Resistance At	
		LD_{50}	LD_{90}	LD_{50}	LD_{90}	LD_{50}	LD_{90}
TEPP	♂	0.0575	0.11	0.112	0.165	1.9	1.5
"	♀	.153	.395	.265	.512	1.7	1.2
Chlordane	♂	.0034	.0063	.38	2.1	111.7	333.3
"	♀	.0165	.0476	4.55	14.87	275.7	312.3
Lindane	♂	.0103	.0155	.0595	.076	5.7	4.9
"	♀	.0242	.0430	.094	.185	3.8	4.3

(8) Vs. *Apis mellifera*:

Insecticide	Oral Dosage (mg × 10^{-5}) For % Kill In 24 Hrs. Shown			Contact Spray (mg/cm² × 10^{-5}) For % Kill As Shown		
	20%	50%	90%	20%	50%	90%
Parathion	1.8	4.0	14.4	25.7	35.4	57.4
TEPP**	5.2	6.5	9.3	35.8	44.5	62.1
Lindane	2.6	7.9	34.6	77.2	85.1	98.6
Dieldrin	22.3	26.9	35.4	38.6	57.5	105.2
Aldrin	18.1	23.9	36.5	32.7	56.2	127.4
Chlordane	83.1	112.2	173.0	380.2	500.0	758.0
Systox®	125.5	147.8	188.4	432.1	512.3	661.9
Dimefox®	125.0	190.5	350.6	1652.0	2317.0	3864.0
Toxaphene®	2512.0	3981.0	8017.0	3673.0	4467.0	5998.0

Bees in Contact For 1 Hr. With Residual Films:					Fumigant Effect Of Films 1 Hr. Exp.	
Material	% Kill 24 Hrs.	Dry Film (mg/cm²)	Field Av. Dose (mg/cm²)	(oz/acre)	% Kill 24 Hrs.	Dry Film (μg/cm²)
Dieldrin	90	0.00009	0.0014	2	100	0.280
"	10	0.00004			0	.074
Aldrin	75	0.00009	0.0014	2	100	.74
"	0	0.00004			0	.074
Lindane	100	0.00028	0.0028	4	100	.44
"	0	0.000074			0	.28
Parathion	90	0.00054	0.0014	2	100	5.0
"	10	0.00018			0	2.8
Chlordane	100	0.0034	0.0112	16	100	3.7
"	12	0.009			0	.37
Systox®	50	0.01	—	—	0	18.5
"	22	0.0068				
TEPP**	8	0.00022	0.0056	8	0	5.5
Toxaphene®	9	0.11	0.0168	24	0	70.0
"	0	0.04				
Dimefox®	0	0.05	—	—	0	74.0

(9) For comparative toxicity vs. acarines consult the tabulations and data under the general treatment titled "Acaricides".

c) Effect on beneficial insects: (Also consult section titled Bees and Insecticides.)

  (1) Hazardous to Apis mellifera. High contact toxicity; residues may kill foraging bees 2 days after application to blooming plants. 909, 927 429,1718

d) Pharmacological, pharmacodynamic, physiological, etc.; insects:

  (1) Entrance to insect body: Ready, rapid penetration of insect cuticle; via the cervical membrane of Periplaneta, 50-80% of applied TEPP entered in 5 minutes. 989,2657

    (a) Effectiveness of penetration was influenced by solvent in following order of descending effectiveness: Dioxane > propylene glycol > ethanol > benzene. In the least effective case 68% entered in 1 hour.

  (2) Fate of TEPP in insect body: Labelling of TEPP with P^{32} revealed a swift distribution, generally, through the organism. 5 μg, administered via cervical membrane: (In 60 minutes) 2.4 μg/g in foregut, 0.17 μg/g in midgut, 0.14 μg/g in hindgut, 0.17 μg/g in fat body, 0.041 μg/g in CNS, 0.45 μg/g in blood, 0.41 μg/g in muscle, 0.36 μg/g in balance of body. 989

    (a) Transport by circulation and rate of distribution is a function of water solubility: TEPP > tetraisopropyl pyrophosphate > tetra-n-butyl pyrophosphate > para-oxon.

    (b) Blood concentration declined as TEPP was concentrated in foregut, with secretion into the lumen being unaltered. Fecal P^{32} appeared largely as material(s) inactive vs. choline esterase.

    (c) 90% of TEPP was excreted in 48 hours; in comparison with others, for example para-oxon; rate of elimination was correlated with rate of hydrolysis.

    (d) Via oral intake: TEPP in Periplaneta builds up in crop then diffuses to hemolymph (more slowly than parathion, para-oxon); unaltered in foregut; the P^{32} bearing substances of the hemolymph are inactive vs. choline esterase. TEPP is of relatively low oral toxicity for the roach.

  (3) Mode of action: Signs and symptoms of intoxication (Periplaneta americana): Symptoms imitated those of injected physostigmine; immediate hyperactivity, excessive excitability were followed by exaggerated tonus, muscle incoordination, clonic and tonic convulsions and spasms until death. 505

    (a) Some recovery of insects from the convulsive phase was noted.

    (b) At 3×10^{-7} M, applied to 6th abdominal ganglion of eviscerated Periplaneta: Facilitation at the synapse followed by synaptic block; 3×10^{-3} M was needed to block axon conduction. 2682,2683

    (c) Homogenates of thoracic nerve system of Locusta migratoria migratorioides can hydrolyse acetylcholine and o-nitrophenyl acetate, indicating presence of an esterase; the hydrolysis is inhibited by TEPP. Good correlation between in vitro activity vs. nerve cord acetyl esterase(s) and contact toxicity to aphids is reported. 1584 1755

    (d) Tenebrio molitor (larvae) contain a non-acetylcholine-hydrolyzing esterase which does hydrolyze ethyl butyrate and o-nitrophenyl acetate. TEPP inhibited this esterase. In 5 other insect species (eggs, active stages) a similar enzymic activity was also inhibited by TEPP. Concentration for inhibition of this enzymic action was close to that required for insect ChE inhibition. A sufficient correlation of relative esterase inhibition activity and contact toxicity for insects suggested interdependence of these factors. 2043 1755

    (e) A comparison of ChE inhibition activity and toxicity for TEPP, parathion: TEPP is the more potent enzyme inhibitor but for the following insect species parathion (because of the relative instability of TEPP) is the more potent insecticide: Diataraxia oleracea (eggs, larvae), Ephestia kühniella (eggs, larvae), Plutella maculipennis (larvae), Tenebrio molitor (larvae), Macrosiphum euphorbiae, Acyrthosiphum pisi.

    (f) At 1 μg by injection, Blattella germanica: Immediate increase in oxygen consumption which gradually rose to 3 times the normal rate in 100 minutes, then gradually declined pari passu with the onset and deepening of paralysis until death. TEPP, notably among organic phosphates at 10^{-3}, 10^{-5} M, stimulated in vitro preparations of Periplaneta (♂) coxal muscle cytochrome oxidase as measured by O_2 uptake in Warburg's apparatus. 1441,2305

  (4) Speed of toxic action of TEPP compared with other compounds when used as dusts in talc, applied by dusting tower to Macrosiphum pisi on Vicia faba: 520

Insecticide	Concentration (%)	Temp. (°F)	Time Required For			
			50% Kill		98% Kill	
			hrs.	min.	hrs.	min.
TEPP	0.18	74	0	20	0	56
Toxaphene®	5	72	13	20	19	1
Chlordane	5	72	9	24	18	8
EPN®	0.86	74	5	26	8	6
Dieldrin	1	75	4	7	6	43
Aldrin	1	75	3	44	7	32
DDD	5	72	2	34	4	35
Methoxychlor	10	75	2	1	5	34
Parathion	1	70	1	8	1	43
Parathion	2	70	1	21	1	53
DDT	5	72	0	57	1	45
Lindane	1	72	0	56	1	54
Rotenone (5%, 10% other extractives)	5	72	0	47	1	23
Nicotine	1	72	0	15	1	12
Nicotine	3	72	0	12	0	50
Talc Control	100	67-72	13	28	23	51

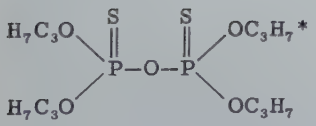
(5) Effect of pyrophyllite (dust diluent) on toxicity of TEPP to Tetranychus bimaculatus (active stages) on bean plants: 2216

Dilution Of TEPP	% Mortality		
		Pyrophyllite	
	No Dust	Before Treatment	After Treatment
1 : 5000	100	6	1
1 : 10,000	100	4	5
1 : 20,000	100	3	2
1 : 40,000	86	2	3
1 : 80,000	43	2	1

e) Field reports; effectiveness of TEPP in control of economic insects:
(1) Vs. phytophagous mites: Excellent acaricide but did not kill mite eggs. 2706
(2) Vs. Cicada (= Magicicada) septendecim: Has controlled infestations of orchards; 90% control re- 126, 676
ported at 0.15% spray; multiple sprayings needed where reinfestation from the wild occurred. 3366, 676
(3) Vs. Chromaphis juglandica: One of best control agents for. 2257
(4) Vs. Brevicoryne brassicae: Yielded good control of. 1137
(5) Vs. greenhouse aphids: 1 mg/ft³ aerosol killed all species. [2871,2868,2872,2873.]
(6) Vs. Myzus persicae: Successful for late infestations on tobacco. 353
(7) Vs. Colias eurytheme: On alfalfa; effective as a dust. 2902
(8) Vs. Argyrotaenia velutinana (larva): Valueless in control of. 1199
(9) Vs. Musca domestica: Laboratory tests at 0.5% in sugar or molasses solution baits yielded 53% kills in 30 minutes, 56% kills in 1 hour, 100% kills in 24 hours. 1915
(10) Vs. Psylla pyri: As an autumn spray vs. last larvae of season, hibernating adults under conditions of Versailles, France, treatments applied in 1st half of October by motor spraying at 12 k/cm² pressure, 13% active ingredient preparation at 0.15% in diluted spray gave a coefficient of efficacity of 12.8% compared to parathion 100, lindane 98.7, DDT 27.7, summer oil + rotenone 56.6, summer oil + nicotine 31.9, summer oil alone 14.9. 2275

180

TETRA - n - PROPYL DITHIONOPYROPHOSPHATE (Tetro-propyl dithiopyrophosphate; Tetra - n - propyl dithiopyrophosphate; NPD; E - 8573.)



* $C_3H_7 = —CH_2CH_2CH_3$

Molecular weight: 378.426

GENERAL (Also consult TEPP, HETP, Sulfatep) [Refs.: 353, 2231, 2773, 1794, 2120, 3106, 854, 830]

An insecticide related to TEPP which is the n-propyl-analogue of tetraethyl dithionopyrophosphate (Sulfatep). The substance belongs to the general class of modern insecticides commonly referred to as organic phosphates or ''organophosphorus'' insecticides. With respect to its close relatives, NPD shows a much reduced mammalian toxicity and in some instances, at least, a very much reduced insect toxicity. However, it possess, in addition to a marked contact and fumigant toxicity for insects, some residual properties. In this last NPD differs sharply from both TEPP and Sulfatep. Has been reported to be equally effective compared with malathion in the residual control of flies, notably DDT-R Musca domestica, in dairies. Reported to be especially effective as a contact and fumigant toxicant vs. aphid species. The closely similar tetraisopropyl dithionopyrophosphate whose properties resemble closely those of NPD may be mentioned here.

PHYSICAL, CHEMICAL [Refs.: 2773, 3106, 2231, 2120]

Technical: An amber liquid; b.p. 148°C at 2 mm Hg; $n_D^{25^\circ}$ 1.4712; volatile; virtually insoluble in water; miscible with most organic solvents, for instance, alcohols, esters, ethers, ketones, aromatic hydrocarbons, methyl chloride; relatively insoluble in kerosene and aliphatic oils; stable under ordinary storage conditions; not readily hydrolyzed in aqueous solution or in presence of moisture; compatible with commonly employed pesticides.

a) Formulations: As a wettable powder, 25%; as an emulsifiable concentrate.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) An inhibitor of choline esterase(s) in vivo and in vitro. 3106
   b) Quantitative:

Animal	Route	Dose (mg/k)	Dosage	
Rat	or	LD_{50}	1450	854
Rat	ip	LD_{50}	1100	854

The above oral LD_{50} for rat may be compared with the following:

TEPP:	1.2-2	Sulfatep:	5	OMPA:	10	Diazinon:	220-270
Para-oxon:	3-3.5	Parathion:	6-15	Potasan®:	19	Dipterex®:	450
BFPO:	3-5	Systox®:	9.4	EPN:	12-40	Chlorthion®:	1500
Malathion:	1400-5834						

(1) Rats, receiving 25 mg/day in the diet, are reported to have suffered growth inhibition. 830

2) Pharmacological, pharmacodynamic, physiological, etc.; higher animsls:
   a) Consult the general treatment titled Organic Phosphates.

3) Phytotoxicity:
   a) Reported to be non-phytotoxic at the concentrations insecticidally effective. 2120

4) Toxicity for insects:
   a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Aëdes nigromaculis (4th instar) DDT-R	Medium	LC_{50} 24 hr.	0.0625 ppm	EPN®=.00086 ppm, Malathion=.025 ppm, DDT=.0588 ppm.	1193
Apis mellifera (adult)	Topical	LD_{50}	200 μg/g	Tetrapropyl dithionopyrophosphate.	2231
Culex tarsalis (4th instar) DDT-R	Medium	LC_{50} 24 hr.	0.0178 ppm	EPN®=.000649 ppm, Malathion=.0185 ppm, DDT=.111 ppm.	1193
Musca domestica (adult)	Topical	LD_{50}	15 μg/g	Tetrapropyl dithionopyrophosphate. .	2231
Musca domestica (adult)	Contact Spray	LC_{50} 24 hr.	0.69 mg/cc	KD 10 min.=0; turntable-Peet-Grady method.	2033
Anopheles quadrimaculatus (4th instar)	Medium	LC_{94} 24,48hr.	0.1 ppm	0.025 ppm gave 62% kill, 0.01 ppm 30% kill.	1766

   b) The above Topical LD_{50} doses for Apis and Musca may be compared with the following: 2231

Insecticide	LD_{50} Topical For (μg/g)	
	Apis	Musca
TEPP	1.2	—
Parathion	1.47; 3.5	0.9
Para-oxon	0.6	0.5
Methyl parathion	1.7	1.0
Chlorothion®	—	16.5
Malathion	—	28
Diazinon	—	4.6
EPN®	3.0	1.9
Sulfatep	5.0	5.0
DFP	30	15

   c) As a bait, 1% in sugar or molasses solutions, in laboratory tests NPD is reported to have yielded 36% kills in 30 minutes, 40% kills in 1 hour, 90% kills in 24 hours. 1915
   d) Used as a spot treatment Vs. Haematopinus eurysternus on cattle, at a concentration of 0.05%, reported to have given 100% kills in 24 and 48 hours remaining effective against reinfestation for 1 week. 2862
   e) Comparative toxicity of NPD others vs. insects:
      (1) For comparative toxicity vs. Anopheles quadrimaculatus and A. crucians in laboratory and field tests consult the last tabulation under Tetraethyl dithionopyrophosphate.
      (2) Vs. Musca domestica (adult) as contact spray; applied by a turntable modification of the Peet-Grady method: 2033

Insecticide	mg/cc To Yield 50% Kill In 24 Hrs.	KD 10 Minutes At LC_{50} 24 Hrs.
Tetrapropyl dithionopyrophosphate	0.69	0
Dieldrin	.017	0
Parathion	.02	0
Methyl parathion	.025	0
Lindane	.046	0
Heptachlor	.052	0
Aldrin	.056	0
TEPP	.069	ca.70%
Chlordane	.25	0
DDT	.35	0
Malathion	.48	0

(2) Vs. Musca domestica (adult) as contact spray; applied by a turntable modification of the Peet-Grady method: (continued) 2033

Insecticide	mg/cc To Yield 50% Kill In 24 Hrs.	KD 10 Minutes At LC_{50} 24 Hrs.
Toxaphene®	.68	0
Dilan	.72	ca.30%
Isolan	1.15	100%
Allethrin	1.5	100%
Pyrolan	5.5	100%

(3) Vs. Culex tarsalis (DDT-R biotype) 4th instar larvae at 70°F and 90°F; average of 6 replications; Laboratory tests: 1193

Insecticide	PPM	% Mortality 24 Hrs. At	
		70°F	90°F
NPD	0.033	44	100
"	.025	17	100
"	.0167	15	85
EPN®	.00067	57	91
"	.0005	46	79
"	.00025	16	48
"	.0000125	4	24
Malathion	.033	24	85
"	.025	19	75
"	.0167	8	40

Field tests vs. C. tarsalis and Aēdes nigromaculis (DDT-R biotypes); Average of 2-5 replications:

Insecticide	Form	A. nigromaculis		C. tarsalis	
		Lbs./acre	% Kill 24 Hrs.	Lbs./acre	% Kill 24 Hrs.
NPD (by jeep)	Emulsion	0.4	93	0.3	99
" " "	"	.3	89	.2	77
" " "	"	.2	87	.1	76
EPN® (by airplane)	Emulsion	.045	98	.045	96
" " "	"	.035	89	.035	89
" " "	"	.025	45	.025	57
EPN® (by jeep)	Emulsion	0.035	99	0.035	100
" " "	"	.025	95	.025	98
" " "	"	.01	89	.01	97
" " "	"	—	—	.005	57
" " "	Suspension	.035	99	.035	100
" " "	"	.025	98	.025	100
" " "	"	.01	55	.01	97
" " "	"	—	—	.005	70
Malathion (by jeep)	Emulsion	.4	99	.3	83
" " "	"	.3	92	.2	97
" " "	"	.2	83	.1	67

As Acaricide

(5) For comparative toxicity of NPD and other compounds as acaricides consult the tabulations and data in the general treatment titled Miticides or Acaricides in this work.

181

THALLIUM SULFATE (Thallous sulfate)

$Tl_2 SO_4$ Molecular weight: 504.85

GENERAL

[Refs.: 851, 353, 129, 2815, 1059, 757, 2226, 1221, 484]

Thallium sulfate, which has been characterized as an excellent rodenticide of moderate hazard (as compared for instance to Warfarin® [low hazard] and sodium monofluoroacetate (compound 1080) [great hazard] has found employment in various syrups and baits for the control of ants. Thallium is one of the most toxic of the elements, being particularly hazardous from the chronic and cumulative stand point. The toxic effects are considered severe, cumulative and similar to those of lead. Thallium is fully as dangerous as arsenic or lead. Some states, (California) prohibit the sale or possession of thallium salts, with certain exceptions. California permits the sale of ant poisons containing no more than 1% thallium. Baits, containing thallium, are often brilliantly colored to minimize the possibility of confusion with comestibles. Thallium acetate has been used in field baits to control the fire ant, Solenopsis geminata. The acetate of thallium has also been employed (too frequently with disastrous results) as a depilatory for cosmetic purposes and in treatment of scalp ringworm.

PHYSICAL, CHEMICAL

A colorless crystalline solid or a white powder; m.p. 362°C; odorless; b.p.: Decomposes before boiling; d 6.77; v.p. very low; solubility in water: 2.7 g/100 g at 0°C, 18.45 g/100 g at 100°C, 4.87 g/100 g at 20°C.

a) Formulations: Usually as sweet syrups or jellies at 0.5% or 1% strength for ant control or at 1% or 1.5% in grain baits for rodents.

TOXICOLOGICAL

1) Toxicity for higher animals:

a) All the actions of thallium are to be classified as toxic. Thallium is readily absorbed from the gastrointestinal tract. When applied in depilatory ointments to the skin it enters the circulation. In the body, thallium is widely distributed and very slowly excreted over months by the kidneys and intestine. Thallium is cumulative. Essentially, all thallium poisoning appears to be chronic poisoning, similar to lead poisoning. Acute toxicity follows, ordinarily, only relatively massive doses. The element is regarded as being more toxic than lead. The element tends to concentrate in liver, brain and skeletal muscle. Ca. 70% of a given dose is excreted in 1 month. 851,1221 1520

(1) Hazard for man: Of 778 cases reported in a review of thallium poisonings in 1934, 6% of the reported cases were fatal. The hazard lies in therapeutic use as a depilatory, in accidental ingestion of thallium-containing salts, pesticide formulations and industrial exposures. 2320,1221

(2) Hazard for animals: Since thallium salts, particularly the sulfate, are used as rodenticides for rats, mice, ground squirrels, prairie dogs, etc., the hazard, under proper conditions of exposure, is apparent. In tests of thallium salts on the moulting mechanism of chickens, the acetate was found more toxic than the sulfate, carbonate or fluoride. 50 cc per day of a 400 ppm solution (20 mg) of thallium acetate killed in 11 days; 10 mg per day in water killed in 19 days. Young birds died in 11 weeks of chronic poisoning caused by daily doses varying from 0.05 mg for two day old birds to 6 mg for 7 week old birds. 1905

(3) Fatal dose for man is reported as $<$ 500 mg thallium sulfate. 129

b) Quantitative:

Thallium Salt	Animal	Route	Dose	Dosage (mg/k)	Remarks	
Thallium sulfate	Rat	or	LD_{50}	25		2636,1951
" "	Rat (Norway)	or	LD_{50}	15.8 ± 0.9		790
" "	Rat (White)	or	LD_{50}	22.9	Death in 3-4 days.	803
" "	Sheep	or	Min. Toxic Dose	8	Single, oral dose.	2377
Thallium acetate	Mouse	sc	MLD	0.5		1041
" "	Rabbit	sc	MLD	5	Death in 7 days.	1041
" "	Dog	or	MLD	18.5	Death in 9 days.	1041
" "	Bird	sc	LD	40-160		1041
Thallium nitrate	Rat	sc	LD	20	Death in 48 hours.	1041
" "	Rabbit	iv	LD	14		1041
" "	Dog	or	LD	45	Death in 4 days.	1041

c) Chronic toxicity:

(1) The chronic hazard of thallium is emphasized by all who have dealt with the substance therapeutically or toxicologically. 851,1221

(2) Characteristic of chronic poisoning is complete loss of body hair, with potentially severe 2322,1221, 851

damage to many organs notably the central nervous system. The depilatory action is reversible, unless the administration has been prolonged unduly, normal hair growth is resumed. The strip of hair across the forehead is often spared.

(3) With small or sub-acute doses symptoms may appear in a week or two, with death in several weeks. In non-lethal dosage, recovery may be complete.

d) Pharmacological, pharmacodynamic, physiological, etc., higher animals:

(1) The mechanism leading to depilation is unknown. 1221

(2) An action on the sympathetic nervous system augmenting normal response to stimulation has been suggested. 810

(3) No evidence of a once-postulated selective action on endocrine glands has been found in rats. 621

(4) Other sites of action of importance include the circulation and CNS. 851,1221

(5) Symptoms of poisoning: Referable chiefly to nervous system and gastrointestinal system, with an onset of 12-24 hours after a toxic dose. Severe, paroxysmal abdominal pain (toxic effect on capillaries of the gastrointestinal tract after absorption) vomiting and diarrhoea. Hemorrhage and desquamation of intestinal mucosa are notable. Stomatitis is frequent; may be ulcerative. Gingival line, as in other heavy metal poisonings is apparent. In chronic poisoning the gastrointestinal signs are not severe. Nervous symptoms include: Paresthesia of hands and feet. Lesions are not confined to the peripheral nerves. Retrobulbar neuritis is common in chronic poisoning with damage which may be permanent. Ptosis, strabismus, mydriasis and facial palsy may be present. In severe acute cases: Delirium, convulsions and death in respiratory failure. Central necrosis of liver lobules, glomerular damage in kidney and tubule degeneration may be present in chronic poisoning. Skin changes: Various eruptions, keratinization, ecchymoses and petechiae. 851,1221

2) Toxicity for insects:

a) Used in syrups vs. Monomorium pharaonis (Pharaoh's ant) which is difficult to control with arsenic. 2523

b) For control of Solenopsis geminata: 3113,3112,3111

Thallium acetate	as 1% baits in bait cans	86% of treated colonies destroyed.*
Thallium sulfate		90% " " " "
Thallium acetate	as 1% baits all methods of application	94% " " " "
Thallium sulfate		88% " " " "

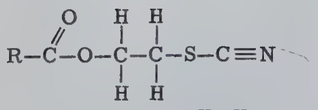
* at end of 2 months, 20 g bait per colony.

c) Mortality of caged crickets, Gryllus assimilis, supplied with thallium sulfate baits (Bran 100 g, water 95-105 cc + amount of thallium sulfate and other ingredients indicated.):

Toxicant	Amount (g)	Other Ingredients	% Mortality At		
			24 hrs.	48 hrs.	72 hrs.
Thallium sulfate	4	Molasses 16 cc	6	20	44
Sodium fluosilicate	5	" "	30	66	84
" "	12	" "	59	86	92
Sodium fluoride	5	" "	30	66	84

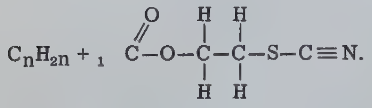
182

2-THIOCYANOETHYL ESTERS OF C_{10}-C_{18} ALIPHATIC ACIDS
(Lethane® 60; β-Thiocyanoethyl laurate.)



$R-C(=O)-O-CH_2-CH_2-S-C\equiv N$

where R = $C_{10}H_{21}$ to $C_{18}H_{37}$, or



$C_nH_{2n+1}C(=O)-O-CH_2-CH_2-S-C\equiv N.$

Also Lethane® Special, a mixture of 2-Butoxy-2′-thiocyanodiethyl ether, and Lethane® 60 1 : 3 v/v.

GENERAL

(Also consult 2-butoxy-2′-thiocyanodiethyl ether, lauryl thiocyanate, Thanite® and the section titled Thiocyanates, Thiocyanacetates.) [Refs.: 353, 2231, 2815, 1059, 757, 2120, 1429, 130, 414, 418, 314, 1828, 3261, 2078, 851]

The thiocyanate insecticides are characterized by the ability to bring about rapid "knockdown" of insects. Thus, they have been used as pyrethrum replacements in various sprays for house and livestock insects. As a class, these compounds and their formulations are very toxic to aphids (lethal toward aphid eggs also) whiteflies, thrips, mealy-bugs and leaf hoppers. Lethane® 60 is a quick-acting, contact insecticide of a low toxicity for mammals and higher animals in general. Used in control of human body lice, Pediculus humanus corporis, the compound has been found irritating to the skin.

PHYSICAL, CHEMICAL [Refs.: 2694, 129, 2120]

Amber yellow, mobile liquid (the product marketed as Lethane® 60 consists of a minimum of 50% by weight of the esters named above in kerosene solution) b.p. 190°C; $d^{25°}$ 0.89-0.915; not soluble in water; soluble in organic solvents such as petroleum oils, kerosene; flash point not less than 125°F; slight "organic" odor; oily taste; may separate at freezing temperature; stable.

TOXICOLOGICAL

1) Toxicity for higher animals:
   - a) While relatively low in toxicity the thiocyanate insecticides kill rapidly when administered at the lethal dosage. All may be absorbed via the skin at toxic levels and the various Lethanes® are irritating to the skin. 1949 2078 851
     - (1) Lethane® 60 is deemed dangerous when applied to the unbroken skin at 500 mg/k. 1860,1949,3201
     - (2) The thiocyanates of the aliphatic series act on the CNS as paralytic toxicants without narcotic action. The lower members of the series yield HCN in vivo and may asphyxiate on inhalation. The higher homologues are more stable with damage being concentrated in the liver. 1214,1304, 1949,3062
   - b) Symptoms of organic thiocyanate intoxication: Restlessness, followed by profound depression, cyanosis, dyspnoea and tonic convulsions. 1951
     - (1) Death is due to respiratory paralysis.
   - c) With 2-butoxy-2′-thiocyanodiethyl ether which is a component with Lethane® 60 of Lethane® Special, pathological signs have been observed which included vacuolation of hepatic cells and a pneumonitis of monocytic and fibrinous type. 2078
   - d) Quantitative:

Animal	Route	Dose	Dosage	Remarks	
Rat	or	LD_{50}	ca. 500 mg/k	Death swift at fatal dosage.	1951,1949
Rat	or	LD_{50}	0.7 cc/k	" " " " "	2078
Rat	ip	LD_{50}	0.16 cc/k	" " " " "	2078
Rat	sc	LD_{50}	0.5 cc/k	" " " " "	2078
Guinea Pig	or	LD_{50}	0.75 cc/k	" " " " "	2078
Guinea Pig	sc	LD_{50}	0.7 cc/k	" " " " "	2078
Guinea Pig	ip	LD_{50}	0.13 cc/k	" " " " "	2078
Rabbit	or	LD_{50}	0.2 cc/k	" " " " "	2078
Rabbit	ct	LD_{50}	ca. 10,000 mg/k, 5 cc/k	" " " " "	1952
Rabbit	sc	LD_{50}	0.25 cc/k	" " " " "	2078
Rabbit	ip	LD_{50}	0.2 cc/k	" " " " "	2078
Dog	or	LD_{50}	0.25 cc/k	" " " " "	2078
Dog	sc	LD_{50}	0.625	" " " " "	2078

d) Quantitative: (continued)

Animal	Route	Dose	Dosage	Remarks	
		As Lethane® Special			
Rat	or	LD$_{50}$	ca. 400 mg/k		1951
Rabbit	ct	LD$_{50}$	ca. 1000 mg/k		1952

e) Comparative

"Thiocyanate"	Animal	Route	Dose	Dosage	
Thanite®	Rat	or	LD$_{50}$	ca. 1000 mg/k	1951
"	Rat	or	LD$_{50}$	6 cc/k	2506
"	Guinea Pig	or	LD$_{50}$	2 cc/k	2506
"	Rabbit	ct	LD$_{50}$	6 cc/k	1952
Lethane® 384	Rat	or	LD$_{50}$	ca. 90 mg/k	1951
" "	Rat	or	LD$_{50}$	0.25 cc/k	2078
" "	Rat	sc	LD$_{50}$	0.275 cc/k	2078
" "	Rat	ip	LD$_{50}$	0.045 cc/k	2078
" "	Guinea Pig	or	LD$_{50}$	0.2 cc/k	2078
" "	Guinea Pig	sc	LD$_{50}$	0.225 cc/k	2078
" "	Guinea Pig	ip	LD$_{50}$	0.042 cc/k	2078
" "	Rabbit	or	LD$_{50}$	0.06 cc/k	2078
" "	Rabbit	sc	LD$_{50}$	0.05 cc/k	2078
" "	Rabbit	ip	LD$_{50}$	0.04 cc/k	2078
" "	Rabbit	ct	LD$_{50}$	0.125-0.25 cc/k	1952

2) Phytotoxicity:

a) Reported to be not phytotoxic with the recommended dilutions and methods. 129

b) Lethane® Special is phytotoxic and not recommended for use on plants save as a dormant spray or in the early stages of bud formation.

(1) In general, the phytotoxic hazard of thiocyanates is deemed high.

3) Toxicity for insects:

a) High in contact toxicity for numerous insects when employed as direct sprays; particularly effective vs. aphids (active stages and over-wintering eggs). Noted for rapidity of "knockdown." 130,1429 1236

b) The action is one of rapid paralysis ("knockdown").

(1) Application of the LD$_{50}$, topical to Blattella germanica brought the following train of events: I) Brief excitement II) extension of appendages with violent twitching III) paralysis.

(2) The initial symptoms had as a concomitant a marked decrease in O$_2$ consumption; during the whole stage of intoxication the respiratory rate was ca. 1/2 the normal. A similar phenomenon was reported for Oryzaephilus surinamensis, treated with Lethane® B-71 (β,β'-dithiocyanodiethyl ether as a 13.5% dust). 1441,2041

(3) Application of 2-butoxy-2'-thiocyanodiethyl ether (a component with Lethane® 60 of Lethane® Special was followed in Periplaneta americana (topical application) by immediate decrease in heartbeat and rate of circulation. In the case of a sub-lethal dosage, heart beat and circulation rates rose later, the symptoms being cyanide-like. Histologically, in Musca domestica (adult), destruction, in muscle cells, of nuclear membrane and disintegration of non-fibrous cells of the brain have been noted. 2421,3201 588,3382

c) Both Lethane® 60 and Lethane® 384 (2-butoxy-2'-thiocyanodiethyl ether) showed marked inhibitory action at 10^{-3} M on in vitro Periplaneta americana (♂) coxal muscle cytochrome oxidase preparations as measured by O$_2$ uptake in Warburg's apparatus. 2305

d) Comparative toxicity:

(1) Toxicity of some thiocyanate insecticides vs. Pediculus humanus corporis and Cimex lectularius; contact sprays of the toxicants dissolved in refined white oil (P31) with solvent volume constant at 1 cc; insecticide concentration varied; the spray deposited at 0.36 mg/cm^2, at which the oil vehicle is harmless to insects: 413, 414

Direct Contact Spray	LC$_{50}$ (As % Concentration)		
	Pediculus	Cimex	Ratio
Lethane® 60	8.1	32.0	3.9
Lethane® 384	1.5 (135μg/g insect)	4.0 (450 μg/g insect)	2.7
Lauryl thiocyanate	6.0	19.5	3.2
Thanite®	3.2	75.0	ca. 25
Lethane® Special	2.5	12.5	5.1

(2) Vs. adult Cimex lectularius and Pediculus humanus corporis, Lethane® 60 and other compounds; direct spray tests; the P31 oil solutions of the sprays deposited as 0.36 mg/cm^2 at which the oil diluent is innocuous to insects: 413, 414

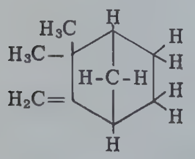
Compound	Pediculus LC_{50} (% Concentration)	Cimex LC_{50} (% Concentration)
Lethane® 60	8.1	32
Lethane® 384	1.5	4.0
Lethane® Special	2.5	12.5
Lauryl thiocyanate	6.0	19.5
Octyl thiocyanate	5.0	—
Decyl thiocyanate	5.0	—
Dodecyl thiocyanate	5.0	—
Tetradecyl thiocyanate	11.0	—
Hexadecyl thiocyanate	18.0	—
Octadecyl thiocyanate	25.0	—
bis-Ethyl xanthogen	6.2	75.0
Benzyl benzoate	22.0	75.0
Pyrethrins (c 0.44% pyrethrins)	34.0	—
" 0.04% + 2% isobutyl undecyleneamide	3.0	—
Thanite®	3.2	75.0
Lindane	0.016	0.051
DDT	0.03	0.56
Pyrethrins	0.47	0.045
Pyrethrins + 2% Isobutyl undecyleneamide	0.038	0.026

183

TOXAPHENE® (Chlorinated camphene; Synthetic 3956 [Hercules Powder Company]; Octachlorocamphene; Alltox; Geniphene; Penphene; Toxakil etc., etc.)

Approximate empirical formula: $C_{10}H_{10}Cl_8$

Toxaphene is the substance which results when camphene is chlorinated to contain 67%-69% chlorine.



GENERAL (Also consult Strobane®, Aldrin, Chlordane, Dieldrin, Endrin, Heptachlor, Isodrin)
[Refs.: 353, 2231, 2451, 2394, 2666, 2549, 1950, 89, 3199, 2120, 129, 1496, 389, 95, 703, 315, 594, 2427, 2444, 2577, 954, 1828, 913, 371, 370, 3214, 2571, 1802, 436, 3261, 851, 2815, 1801]

A potent contact and stomach insecticide classed as a member of the group of toxicants known as the cyclodiene insecticides which also includes aldrin, dieldrin, chlordane, heptachlor, endrin, and isodrin. These compounds are characterized as cyclic hydrocarbons with a high degree of chlorination and a structure which has, as a common feature, an endomethylene-bridge. This group of insecticides has come into widespread use as agricultural insecticides on a grand scale for the control of cotton and other field-crop insects, soil insects and the control of Orthopteran pests, such as grasshoppers, locusts and crickets in cultivated fields, on ranges and in the wild. The group is also employed in the control of household insects and of insects on livestock. Toxaphene possesses, also, acaricidal properties against certain phytophagous acarines, for example the Cyclamen mite. Toxaphene is not as well characterized chemically as the other cyclodiene insecticides. The precise nature of the compounds present in the mixture of isomers which the name toxaphene covers is not strictly known.

PHYSICAL, CHEMICAL [Refs.: 2231, 3199, 2120, 129, 353, 389, 703, 314]

Toxaphene®, unlike the other cyclodiene insecticides above named, is not produced by the Diels-Alder diene reaction. A yellow to amber, waxy solid with an aromatic, pine-like smell; m.p. 65°-90°C; $d^{27°}$ 1.65; v.p. low, ca. 10^{-6}; non-volatile, loss in weight at 100°C for 20 hours = 0.1%; virtually insoluble in water; not soluble in 95% ethanol; highly soluble in a wide range of organic solvents and oils tending to be more soluble in aromatic than in aliphatic solvents; soluble to 38 lbs./gallon at 80°F in acetone, benzene, carbon tetrachloride, ethylene dichloride; solubility in lbs./gallon at 27°C:

Acetone	> 40
Benzene	> 40
CCl_4	> 40
Ethylene dichloride	> 40
Fuel Oil	20-25
Hexane	> 40
Kerosene (regular)	> 25
Kerosene (deodorized)	> 25
Lube Oil	5-7
Shell E-407	> 25
Solvacide 544C	> 25
Sun Solvent 1547	> 25
Thanite	8-10
Toluene	> 40
White Oil	4-5

In grams/100 cc at 25°-30°

Acetone	>450
Ethanol	12
CCl_4	>450
Benzene	>450
Xylene	>450
Hexane	>450
Mineral Oil	55-60
Isopropyl alcohol	15-18

Not corrosive in absence of moisture at ordinary temperatures; corrosive at high temperatures; stable (but dehydrogenated at high temperatures). May be characterized as a mixture of polychloro-bicyclic terpenes, with chlorinated camphene predominant, containing 67% to 69% chlorine; Dehydrochlorinated by long exposure to sunlight, in alkaline media and above 155°C.

a) Formulations: 10%-20% dusts; 40% wettable powders; emulsifiable concentrates at 4, 6, 8 lbs./gallon; baits e.g. 1% in bran; various solutions. Generally employed for insect control at 1.5-2.0 lbs./acre, e.g. toxaphene is effective in baits against grasshoppers at 1 lb./100 lbs. bran.

TOXICOLOGICAL

1) Toxicity for higher animals:

a) The toxicity of toxaphene is stated to be of about the same order as that of lindane. The dog appears 89,2120
particularly sensitive, and for this animal the oral chronic toxicity is reported as ca. 10 times that of 1950,3199
DDT. The oral lethal dose in oil is variable, presumably because of irregular absorption. 2451,2571

b) Stated to be, for man, a distinctly toxic material which cannot be recommended for household use; very 851
readily absorbed via the skin.

c) The acute LD_{50}, oral, on the basis of "all animals tested": Average = 60 mg/k (DDT = 250, chlordane = 1949
500, DDD = 2500, methoxychlor = 7000, lindane = 125); the danger level for cutaneous application is report- 3199
ed as 780 mg/k. The solvent greatly influences the toxicity of toxaphene.

d) Estimated oral LD for man = 60 mg/k, 2-7 grams/man (4 times the toxicity of DDT). Dermal applica- 2221, 89
tions of 46 g (single dose) or 2.4 g (repeated daily doses) are very dangerous.

e) Toxic to fish at 1 part in 200 million parts. Do not use directly on chickens. 2910,2571

2) Quantitative:

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Mouse	or	LD_{50}	112		809
Rat	or	LD_{50}	ca. 69		1951
Rat	ip	LD	200		2680
Rat, others	iv	LD_{50}	10-15		2231
Rat	or	LC_0	73	5% solution in corn oil.	129
Rat	or	LD_{100}	145	" " " " "	129
Rat	or	LD_0	25	1% " " peanut oil.	129
Rat	or	LD_{50}	40	" " " " "	129
Rat	or	LD_{100}	75	" " " " "	129
Guinea Pig	or	LD_{50}	69		808
Guinea Pig	sc	LD	62.5		2680
Rabbit	or	LD	780		2120
Rabbit	ct	LD_{50}	> 4000	Single acute exposure to dry substance.	1952

2) Quantitative: (continued)

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Rabbit	Immersion	Toxic Dose	1025-1075	Dipping for 2 min. in wett. pwdr.; grooming prevented.	1713
Dog	or	LD_{50}	20-30		2451
Dog	or	LD_{50}	15		1886
Dog	or	LD	50-80	In corn oil; convulsions; death in 3 hrs.	203
Calf	or	Min. Toxic Dose	5	As a single dose.	2567
Calf	Spray, Dip	Min. Toxic Conc.	1.0%	Single spray or dip; suspension or emulsion.	2567
Cattle	Spray, Dip	Min. Toxic Conc.	4.0%	" " " " " " "	2567
Sheep	or	Min. Toxic Dose	25	As a single dose.	2567
Sheep	Spray, Dip	Min. Toxic Conc.	4.0%	Single spray or dip; suspensions or emulsions.	2567
Sheep	iv	LD	5		2680
Pig	Spray, Dip	Min. Toxic Conc.	>4.0%	" " " " " " "	2567
Horse	Spray, Dip	Min. Toxic Conc.	>1.5%	" " " " " " "	2567
Goat (adult)	or	Toxic Dose	50		3199
Fish	Medium	LC	<0.036 ppm		3050,3232
Fish	Medium	LC	1-10 ppm		1192
Fish	Medium	LC	<0.04 ppm		2026
Fish	Medium	LC	0.005-0.01 ppm		353, 215
Trout	Medium	LC	0.01 ppm		2026
Trout (fingerling)	Medium	Toxic Dose	2 ppm*, 8 ppm**	*In velsicol sol.; **In acetone sol.	1937
Bluegill	Medium	Threshold Conc.	0.01 ppm		1937
Bass	Medium	Toxic Conc.	0.05-0.2 ppm	As toxaphene dust.	1937
Bluegill	Medium	Toxic Conc.	0.05-0.2 ppm	" " "	1937
Rainbow Trout	Medium	LC	1-10 ppm	15 minutes exposure.	1192
Goldfish	Medium	Toxic Conc.	0.05-0.2 ppm	As toxaphene dust.	1937
Goldfish	Medium	LC_0	0.0032 ppm	10 days exposure.	828
Goldfish	Medium	LC	0.0056 ppm	Death of most of subjects in 10 days.	828
Goldfish	Medium	LC_{100}	0.01 ppm	Death within 10 days.	828
Goldfish	Medium	Turnover Conc.	0.025 ppm	Turnover in <24 hrs.	828
Frogs, Salamanders	?	LC	1.5 lbs./acre	As toxaphene dust.	353
Sheep, Goat	or	LD_{50}	ca. 200		353
Dog, Cat	or	LD	60	Death in 3 hours.	353

(1) Toxicity of toxaphene, oral route, for farm animals: 2573

XE-65 = toxaphene 65%, xylene 25%, Triton X-100 10%;
KE-65 = toxaphene 65% in kerosene;
WP-40 = wettable powder of 40% toxaphene content.

Animal	No. Of Animals (Total)	Toxaphene® (mg/k)	Formulation	Results	No. Of Animals
Calf (3 months)	3	25	XE-65	No effects	1
			KE-65	No effects	1
			WP-4	No effects	1
Calf (3 months)	3	50	XE-65	Death	1
			KE-65	Affected	1
			WP-40	Affected	1
Goat (adult)	3	50	XE-65	Affected	1
			KE-65	Affected	1
			WP-40	Affected	1
Goat (adult)	3	100	XE-65	Affected	1
			KE-65	Affected	1
			WP-40	No effect	1
Goat (adult)	3	170	XE-65	Death	1
			KE-65	Affected	1
			WP-40	Affected	1
Goat (adult)	3	250	XE-65	Death	1
			KE-65	Death	1
			WP-40	Death	1
Sheep (adult)	3	50	XE-65	No effect	1
			KE-65	No effect	1
			WP-40	No effect	1
Sheep (adult)	3	100	XE-65	Affected	1
			KE-65	Affected	1
			WP-40	Death	1
Sheep (adult)	3	170	XE-65	Affected	1
			KE-65	Affected	1
			WP-40	Affected	1
Sheep (adult)	3	250	XE-65	Death	1
			KE-65	Affected	1
			WP-40	Death	1

As sprays, applied to suckling calves:

No. Animals Total	Toxaphene® Conc. (%)	No. Treatments	Formulation	Results
3	8.0	1	XE-65	Death 1 animal.
			KE-65	Death 1 animal.
			WP-40	Affected 1 animal.
3	4.0	1	XE-65	Affected 1 animal.
			KE-65	No effect 1 animal.
			WP-40	Affected 1 animal.
12	1.5	2	XE-65 (4 animals)	Affected 2, no effect 2.
			KE-65 (4 animals)	Death 1, affected 2, no effect 1.
			WP-40 (4 animals)	Affected 3, no effect 1.
11	1.0	1	XE-65 (8 animals)	Death 1,no effect 7.
			WP-40 (3 animals)	No effect 3.
12	0.75	8	XE-65 (4 animals)	Affected 1, no effect 3.
			KE-65 (4 animals)	No effect 4.
			WP-40 (4 animals)	No effect 4.

As Sprays, Dips; adult animals:

Animal	Conc. Toxaphene® (%)	Total No.	Treatments	Formulation	No. Animals	Results
Steer	8	1	1	XE-65	1	Affected.
Steer	4	20	1	XE-65	7	Affected 1, no effect 6.
				KE-65	6	No effect 6.
				WP-40	7	No effect 7.
Goat	8	3	1	XE-65	1	Death.
				KE-65	1	Death.
				WP-40	1	Affected.
Goat	4	3	1	XE-65	1	No effect.
				KE-65	1	No effect.
				WP-40	1	No effect.
Sheep	8	3	1	XE-65	1	Affected.
				KE-65	1	Death.
				WP-40	1	Affected.
Sheep	4	3	1	XE-65	1	Affected.
				KE-65	1	Affected.
				WP-40	1	No effect.

3) Comparative toxicity, Toxaphene® and other compounds for higher animals:

a) Toxicity to Rabbits, immersed for 2 minutes in wettable powder formulations; animals prevented from subsequent grooming, and thus from oral intake: 1713

Insecticide	Dosage (mg/k)	Results
Toxaphene®	1025-1075	From all the insecticides similar symptoms: Loss of appetite, extreme nervousness, convulsions, wild running, falling and kicking and with muscle spasms each lasting 3-10 minutes.
Aldrin	15-25	
Dieldrin	400-450	

b) Feeding experiments with dogs; Toxaphene® and other compounds: 203

Insecticide	Dosage (mg/k) Active Ingredient	Total Dosage (mg)	Estimated Total (mg) Active Ingredients	Sex	Results
Toxaphene®	20	636	159	♂	Convulsions extreme salivation in 12 hrs.
"	30	1008	252	♂	Convulsions, tremors, diarrhoea in 2 hrs.
"	40	1017.6	254.4	♀	Convulsions, tremors in 12 hrs.
"	50	1544	386	♀	Convulsions, death in 3 hrs.
"	60	2289	572.4	♂	Convulsions, death in 2 hrs.
"	70	2226	556.5	♂	Convulsions, death in 3 hrs.
"	80	2035.2	508.5	♀	Convulsions, death in 3 hrs.
BHC, tech. 33-36%	100	6504	2168	♂	No effect.
γ-isomer	200	12,816	4272	♂	No effect.
"	300	12,681	4227	♂	Slight diarrhoea, nervousness, dilated pupils.
"	400	11,160	3720	♂	No effect.
BHC wettable powder	5	1188.7	71.35	♀	No effect.
" " "	10	2685	159	♂	No effect.
" " "	15	1699	102	♂	No effect.
" " "	20	4389.6	263.6	♂	No effect.
BHC, 6% γ-isomer	25	5110.5	306.8	♀	No effect.
	50	13,245	795	♂	No effect.
	60	13,165	791	♂	Slight diarrhoea, vomiting, anorexia.
	75	8,497	510	♂	No effect.
Chlordane wettable powder	200	7224	3862	♂	Clonic spasms in 12 hrs.

b) Feeding experiments with dogs; toxaphene and other compounds: (continued) 203

Insecticide	Dosage (mg/k) Active Ingredient	Total Dosage (mg)	Estimated Total (mg) Active Ingredients	Sex	Results
50% active ingredients	225	5931	2065	♀	No effect
	250	5110	2555	♀	Respiration slowed.
	300	11,586	5793	♂	Clonic spasms, tremors in 4 hrs.
	400	10,544	5272	♀	Tremors, salivation, convulsions, blindness.
	500	10,220	5110	♀	Tremors, convulsions, prostration.
	700	6356	3178	♂	No effect.

4) Sub-acute, sub-chronic and chronic toxicity:
- a) Toxaphene is deemed reasonably safe as a farm livestock spray; dips are apparently hazardous. 2571
  - (1) Most dangerous, as an acute poison, to young calves.
  - (2) Adult sheep, goats, horses, pigs, tolerated 2.0% concentrations.
  - (3) Cattle treated 10 times with sprays at 2.0% showed no symptoms.
- b) Reported to have little tendency for storage in the animal body. 2571
  - (1) Steers, sheep fed at 10 ppm in the diet showed no toxaphene in fat on 30th day of exposure.
  - (2) Reported to have been found in milk of cows, receiving toxaphene treated hay at 2.3-2.5, 4.3-3.9, 8.3-18.2 ppm (hay treated in field at 1, 2, 4 lbs/acre. 200 26
  - (3) Steers, cattle, lambs, sheep fed on alfalfa sprayed twice at 2 lbs./per acre showed 300 ppm in fat, 7 ppm in lean meat; at 1 lb. per acre sprayed alfalfa 25 ppm and 1 ppm were recovered in fat and lean meat respectively. 791
- c) Toxaphene® by inhalation:
  - (1) Mouse LC_{50} for 2 hour exposures = ca. 0.2 mg per 100 cc of air per minute. 583
  - (2) Intratracheal 0.5% toxaphene emulsion in water reported not to have aroused symptoms referable to toxaphene. 2573
- d) Dermal hazard:
  - (1) Readily absorbed by skin. Rabbits, Guinea pigs proved more susceptible than dogs. 353
  - (2) Dusts stated to present no skin hazard. 353
  - (3) Oil solutions and liquid formulations penetrate skin more readily than dusts or wettable powders. 89
  - (4) Moderately irritating to human skin, but without evidence of sensitization. 353
  - (5) For cattle and calves 0.5% emulsion dips or sprays produced no injury; 2 dips in 2.5% emulsions yielded toxic symptoms; 8% emulsions proved fatal, but recovery followed 8% suspensions; 4% emulsions presented toxic hazard to sheep, but had no effect on cattle in single dips.
  - (6) Repeated dermal application to Rabbit at 40 mg/k led to death within a short time of 50% of the subjects. 2231
- e) Chronic feeding experiences:
  - (1) Tolerated in diet by Cattle sans symptoms at 1200 ppm. Steers and lambs on alfalfa sprayed at 8 lbs. per acre showed temporary nervous symptoms. 2109
  - (2) Dairy cows, on daily doses of 2.5-37.5 g (6.3-93.8 mg/k per day) as wettable powder, showed no toxic effects from doses up to 5 grams; 7.5 grams per day for 1-2 weeks caused nervousness, diarrhoea, anorexia, fits and convulsions with symptoms most serious 15 hours after exposure and wearing off in the ensuing 10 hours. 1964
  - (3) Dogs, receiving in the diet 330 ppm, died in ca. 33 days; toxic symptoms ensued at 60 ppm in 2 weeks; at 25 mg/k/day 100% were dead on 1st day. 3199 1953
  - (4) Rats, receiving 800 ppm in diet (as 5% kerosene solution) for 6 months, showed no significant change in weight, hematology, mortality rate and showed no tissue damage. 583
  - (5) Rat: Conflicting reports: At 25 ppm in diet: No effect; at 100 ppm: Liver damage. at 1200 ppm for 8 weeks in diet: No toxic effects; 250 ppm tolerated for 12 weeks. 1953 1949

5) Human poisonings with Toxaphene®:
- a) Cases of poisoning (with recovery upon treatment) after consuming cooked toxaphene-treated leafy vegetables have been reported. 2171
- b) Child fatalities from eating toxaphene insecticides are known. 2171,2521
- c) Stated that spray residues on crops may be limited to 15 ppm by attention to fabricators directions. On alfalfa a residue concentration (initial) of 30 ppm was reduced to 16 ppm in 14 days (half-life = ca. 16 days). 1497, 680
- d) Symptoms in non-fatal cases included: Clonic-tonic convulsions, tonic spasms with unconsciousness, muscular twitching, "light-headedness," gastric distress; in fatal cases: Suddenly, after several hours latent period, convulsions (not preceded or associated with gastro-intestinal disturbances), loss of consciousness, death in a few hours. Autopsy (1 subject): Congestion, oedema of lungs, heart dilation and pin-point haemorrhages of brain were noted. 2171,2521

6) Hazard to wildlife:
- a) Under appropriate circumstances of exposure, the experimental toxicity shown for laboratory and other animals indicates that toxaphene is potentially hazardous to wild warm-blooded animals.
- b) Experimentally, toxaphene is poisonous to various fishes. Well-documented reports indicate extensive kills and damage to fish in the watersheds of streams and tributaries receiving "run-off" from extensive cotton fields treated heavily (in many instances to excess) with toxaphene. Severe damage has been done to fish in farm ponds where dusting to control cotton insects has occurred. 3050,1937 2026,3391
  - (1) In the Tennessee valley of Alabama, in 1950, ca. 26,300,000 lbs. of organic insecticides were used vs. boll weevil on cotton on ca. 420,000 acres in 8 counties (ca. 63 lbs. per acre per season). The most 2720

popular compound was a 20% toxaphene + 40% sulfur dust. Others were DDT, BHC with some aldrin and minor amounts of calcium arsenate. Of the total insecticides used toxaphene comprised 61%, BHC + DDT, 34%, aldrin 4%, others 1%.

(2) Toxaphene® proved the most toxic of these insecticides for fishes; < 0.037 ppm (as solution) killed many fishes in ponds. 3050

(a) Toxaphene® is more toxic to fish than rotenone. 3050

(b) Toxaphene® is more toxic to fish than DDT; young trout were killed at 0.005 ppm; threshold limit for Bluegill = 0.01 ppm; many fishes (not goldfish) were killed at 0.02 ppm. 2026

(c) Toxaphene®, in aquaria, killed bluegill and bass fingerlings at 0.05 ppm as toxaphene dust; goldfish were inactivated in 54 hrs. and killed in 156 hrs. at 0.05 ppm; in an earthen pond 0.05 ppm toxaphene did not kill bluegill, bass or bait-sized goldfish within a 5 week period, but at 0.2 ppm killed all these forms within 45 hrs., the water remaining toxic for at least 10 weeks. In earthen ponds 0.4 ppm DDT killed only recently hatched Pimephales promelas (fat-head minnow); 2 ppm. DDT killed all fish within 48 hrs. 1937

c) Toxaphene® damage to fish is enhanced (as is the hazard) in seasons of heavy rainfall and rapid drain-off, after treatment of large acreages. 3391

(1) Toxaphene® dust is recommended at 10 lbs. per acre (20% dust) applied 6-7 times during normal sea- 2720
son or 12-15 lbs. per acre, with more frequent application in seasons of heavy rain or great insect in- 3391
festation.

(2) In the instances of heavy fish kills on Alabama watersheds, dusts were used in excessive amounts by some cultivators, for instance 40 lbs. per acre or 540-560 lbs. per acre per season (in 16 applications) which, in quick run-off conditions, accounted for kills of fish in a stream of 50 miles length with a mid-channel depth of 6-20 feet (depending on flood stage) and a rather slow current; in this stream fish were probably wiped out. (Flint Creek, in Morgan Co., Alabama.) On the watershed of this stream extensive insecticide use on cotton began in early July. Frequent rains in mid-July brought applications of insecticide at intervals shorter than usual. After a heavy rain on August 1-2, leading to a 6 inch rise in water level, fish on the following morning were seen swimming peculiarly at the surface. By the next day great numbers of dead fish were observed. Caged goldfish placed in the stream were affected within 24 hours. By 18th August a survey revealed dead fish by the hundreds, some ranging to 15 lbs. in weight (Carp, Buffalo, Drum, Gizzard Shad, Catfish, White Crappie, Bass, Sunfish). No such occurrence had ever been reported prior to 1950, the first year of heavy organic insecticide use. The only major change on the watershed was use of such agents (principally toxaphene) vs. boll weevil. No sources of industrial pollution were present and no other source of pollution could be discerned. No cases of human intoxications were reported. Water supplies drawn from affected streams were treated by conventional purification. Fish were directly affected by toxaphene (presumably) and indirectly affected by decimation of the fish-food-organisms. 3391

(3) Summary: Widespread insecticide (by inference toxaphene, the most heavily used) + too frequent showers leading to frequent reapplication with build-up of heavy soil concentrations + heavy August rains resulted in the washing into at least 15 streams of toxicant sufficient to eradicate all fish from some streams and heavily to deplete others. Kills were associated with increases of stream water levels following heavy rains, accompanied by increases in stream turbidity. Such pollutions of streams with organic insecticides may become an increasingly serious problem.

d) Comparative toxicity of Toxaphene® and other compounds to Bobwhite Quail and Mourning Dove; oral administration in gelatin capsules: 679

Compound	Quail				Dove			
	LD_{50} (mg/k)	MLD (mg/k)	Average Wgt. Loss (%)	Average Days Lived	LD_{50} (mg/k)	MLD (mg/k)	Average Wgt. Loss (%)	Average Days Lived
Toxaphene®	80-100	40	25	3	ca.200-250	100	22	3
Aldrin	4-4.5	4	15	3	15-17	12.5	18	4.5
Dieldrin	12-14	10	20	4	44-46	40	15	3
Lindane (♂)	120-130	120	25	3	ca.350-400	200	10	2.5
Lindane (♀)	190-210							

7) Pharmacological, pharmacodynamic, physiological, etc.; higher animals:

a) Toxaphene may be characterized as a general convulsant acting on the CNS to induce diffuse stimulation 89,1886
leading to generalized convulsions. Resembles chlordane (q.v.) and, to some extent, camphor, in physio- 26,2451
logical action. Convulsions are tonic and/or clonic in nature. Death usually occurs in respiratory 583,2569
failure. Against moderate lethal doses pentobarbital sodium is protective.

(1) In dogs and cats single doses (20 mg/k) were convulsant and 60 mg/k led to death in 3 hours.

b) Symptoms of poisoning included: Salivation, vomiting, reflex excitability, epileptiform spasms. Various barbiturates control the convulsions. 26

(1) Symptoms ordinarily begin in experimental animals within 1 hour, and resemble those of camphor. The convulsive symptoms are aggravated by external stimulation and are followed by depression. 89,1886

(2) Death may occur as early as 4 hours and as late as 24 hours after lethal doses. 89

(3) High internal temperatures and internal hemorrhage are reported in calves, sheep, goats. High internal temperature is a symptom in man, also, of camphor poisoning. 89

c) Toxaphene® may enter via all portals. Dermal absorption is particularly easy; liquid preparations pene- 89,2231
trate skin more readily than dusts or wettable powders. 353

(1) Species differences in susceptibility exist, as do age differences, and the solvent and formulation 1886,353
strongly influence toxicity. For example, toxaphene is reported less toxic in kerosene than in corn 3199
oil solution.

(2) Mildly to moderately irritating to the skin. Rabbits readily absorb [in contrast to dogs (which are very susceptible by oral route)] lethal quantities via the unbroken skin from dimethyl phthalate or mineral oil solutions in water emulsion. Single sprayings, as xylene-kerosene + water emulsions (8% toxaphene) killed calves; 2 sprayings at 1.5% concentration yielded toxic effects; single applications at 0.75% proved an MLD dosage, fatal to 1 of 12 calves. 1886,2573

(3) Action is cumulative; repeated oral doses of 4 mg/k occasionally and 5 mg/k regularly induced convulsions after several days. 1886

d) Fate in the animal body:

(1) A slow detoxification in the liver is indicated by excretion of ethereal sulfate and glucuronate. Organic chloride content of brain was enhanced by toxaphene intake. With repeated dosage, storage in fat (accumulation in fat) has been noted and excretion in milk confirmed. 583,1954 2572, 791 1886

e) Pathology:

(1) Degenerative changes (hydropic, ? reversible) of the hepatic parenchyma. Marked degenerative changes in renal tubule epithelium. Possible accumulation of toxaphene in the ascending limb of the loops of Henle. No pathology of brain, skeletal muscle, heart, lungs, adrenals, pancreas, stomach, spleen, intestinal tract is reported. 1886,89 1949

(2) Toxaphene® poisoning (oral and cutaneous) in sheep, goats, calves: Cyanotic mucosae, congestion of brain, spinal cord, lung; heart block in systole; hemorrhage in heart and intestines; congested kidneys; discolored liver. 89

8) Phytotoxicity:

a) The phytotoxic hazard of toxaphene is apparently low. Damage is possible to some Cucurbitaceae known to be sensitive to halogenated hydrocarbon insecticides. 129,2120
(1) May produce "off-color" in cured tobacco.

b) As 0.4% suspension harmless to 70 species of trees or shrubs; exceptions: Sugar maple (Acer saccharum), Imperial Gage plum. 2960

c) As a 25% wettable powder pre-sowing spray at 6.4 lbs. per acre, yielded no injury to seedling tobacco; no residual phytotoxicity in tobacco beds 4 months after treatment. 123

d) Injury to apple foliage caused only when toxaphene was applied in oil; may (in oil) cause russetting, and burning of pear foliage and prune tree leaves. 472

e) Phytotoxic to peach foliage with chlorosis and marginal "burning"; "safened" by wettable sulfur. 2859

f) At 0.1% suspensions injury to potatoes has been reported; at 0.4% suspensions and sprays caused chlorosis of potato foliage. 3142 2450

g) 0.1% suspensions yielded severe injury to death of cucumbers, cantaloupe; 2.5% dusts severely injured squash and Cucurbitaceae generally, especially in case of young plants under conditions of high humidity. 3% dusts yielded 100% kills of Cucurbita pepo and 25% kills of Cucurbita moschata. 2959 482

h) Damaged Zea mays when applied in oil. 3364

i) At 25 lbs. per acre no crop plants were damaged. 2304

j) In some cases depressed growth of seedling plants. 662

k) In the soil toxaphene is decomposed at an appreciable rate of speed by soil micro-organisms. Absorption from the soil into plants does not occur. 663 294,1298

9) Toxicity for insects:

a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	
Anopheles quadrimaculatus (adult ♂)	Topical	LD_{50}	0.15 µg/insect	Relative effectiveness compared to DDT = 0.13.	2051
A. quadrimaculatus (adult ♀)	Topical	LD_{50}	0.29 µg/insect	" " " " " = 0.23.	2051
A. quadrimaculatus (adult ♂)	Topical	LD_{90}	0.29 µg/insect	" " " " " = 0.16.	2051
A. quadrimaculatus (adult ♀)	Topical	LD_{90}	0.5 µg/insect	" " " " " = 0.26.	2051
A. quadrimaculatus (larva)	Medium	MLC_{100}	0.01 ppm	80% mortality at 0.005 ppm.	2020
Anthonomus grandis (adult)	Contact + or	LC_{50}	6.4 % dust	6.4 = % active ingredient as lbs./acre; food plant dusted./	2276
Apis mellifera (adult)	or	LD_{50} (72 hr.)	22.0 µg/bee		910
Apis mellifera (adult)	or	LD_{20} 24 hr.	25.12 µg/bee	Given in 50% sugar solution.	1718
Apis mellifera (adult)	or	LD_{50} 24 hr.	39.81 µg/bee	" " " " " .	1718
Apis mellifera (adult)	or	LD_{100} 24 hr.	80.17 µg/bee	" " " " " .	1718
Apis mellifera (adult)	or	LD_{50} (72 hr.)	31.9 µg/bee		3249
Apis mellifera (adult)	Contact Spray	$LDeposit_{20}$	36.73 µg/cm²		1718
Apis mellifera (adult)	Contact Spray	$LDeposit_{50}$	44.67 µg/cm²		1718
Apis mellifera (adult)	Contact Spray	$LDeposit_{90}$	59.98 µg/cm²		1718
Apis mellifera (adult)	Residue	$LDeposit_{9}$%	0.11 mg/cm²	Average field dose = 0.0168 mg/cm².	1718
Chrysops discalis (adult)	Topical	LD_{50}	180 µg/fly		2707
Chrysops discalis (adult)	Topical	LD_{90}	480 µg/fly		2707
Cirphis unipuncta (larva)	Topical	LD_{50}	56.2 µg/g	Ratio to parathion (=1) = 15.2.	3268
Cirphis unipuncta (larva)	or	LD_{50}	34.1 µg/g	" " " " = 13.6.	3268
Heliothis virescens (6th instar larva)	Topical	LD_{50}	18,000 µg/g	Abdominal application in methyl ethyl ketone.	1124
Heliothis zea (6th instar larva)	Topical	LD_{50}	2000 µg/g	" " " " " "	1124
Locusta migratoria migratorioides (young adult)	Topical	LD_{50} 5 days	140.0±7.6 µg/insect	In oil-cyclohexanone 9 : 1.	1585
Locusta migratoria migratorioides (young adult)	Topical	LD_{50} 5 days	133.0 µg/g	" " " " .	1585
Locusta migratoria migratorioides (young adult)	Topical	LD_{95}	258.0 µg/insect±18.6	" " " " .	1585
Locusta migratoria migratorioides (young adult)	Topical	LD_{95}	245.0 µg/g	" " " " .	1585
Melanoplus differentialis (1st,2nd instar nymphs)	Contact Spray	LD_{50}	0.91 Lbs./acre	Miscible oil formulations.	1102
Melanoplus differentialis (adult)	Topical	LD_{50}	61.0;73.9 µg/g	In dioxane, acetone, ethanol sols.	3267
Melanoplus differentialis (adult)	or	LD_{50}	75.0;91.5 µg/g	As deposit on leaves.	3267
Melolontha melolontha	Topical	LD_{50} 5 days	ca. 7 µg/insect	Relative to BHC(tech) = 1 = ca. 0.1.	3184
Melolontha melolontha	Topical	LD_{80} 5 days	ca. 20 µg/insect	" " " " " = ca. 0.12.	3184
Musca domestica (adult)	Topical	LD_{50}	31 µg/g		2231
Musca domestica (adult)	Contact Spray	LD_{50} 24 hr.	0.68 mg/cc	KD 10 min. at LC_{50} = 0; Turntable method.	2033
Musca domestica (adult)	Topical	LD_{50} 24 hr.	0.22 µg/fly	DDT-non R; at 60°F.	371

a) Quantitative: (continued)

Insect	Route	Dose	Dosage,	Remarks	
Musca domestica (adult)	Topical	LD_{50} 24 hr.	0.62 µg/fly	Bellflower strain, DDT-R; at 60°F.	371
Musca domestica (adult)	Topical	LD_{50} 24 hr.	3.4 µg/fly	Pollard strain; DDT-R; at 60°F.	371
Musca domestica (adult) DDT-non R	Topical	LD_{50} 24 hr.	0.2 µg/fly	Lab strain; DDT-non R; measured drop.	78
Musca domestica (adult) DDT-R	Topical	LD_{50} 24 hr.	0.6 µg/fly	Bellflower strain; measured drop test.	78
Musca domestica (adult) DDT-R	Topical	LD_{50} 24 hr.	0.4 µg/fly	San José strain; measured drop test.	78
Musca domestica (adult) DDT-R	Topical	LD_{50} 24 hr.	0.5 µg/fly	Ontario strain; measured drop test.	78
Musca domestica (adult) DDT-R	Topical	LD_{50} 24 hr.	0.5 µg/fly	Riverside strain; measured drop test.	78
Musca domestica (adult) DDT-R	Topical	LD_{50} 24 hr.	73.0 µg/g	DDT-I (21 generations exp.); in acetone.	373
Musca domestica (adult) DDT-R	Topical	LD_{50} 24 hr.	38.4 µg/g	DDT-W (3 yrs. field exp.); in acetone.	373
Musca domestica (adult) methoxychlor-R	Topical	LD_{50} 24 hr.	38.2 µg/g	Methoxy-I (21 generations exp.) in acetone.	373
Musca domestica (adult) lindane-R	Topical	LD_{50} 24 hr.	66.3 µg/g	Lindane-I (21 generations exp.) in acetone.	373
Musca domestica (adult) Multi-R	Topical	LD_{50} 24 hr.	76.4 µg/g	Multi-I (8 generations exp.) in acetone.	373
Musca domestica (adult) non-R	Topical	LD_{50} 24 hr.	29.16 µg/g	Lab I, NAIDM strain; in acetone.	373
Musca domestica (adult) non-R	Topical	LD_{50} 24 hr.	32.2 µg/g	Lab II, Univ. of Indiana; in acetone.	373
Musca domestica (adult) Toxaphene®-R	Topical	LD_{50} 24 hr.	39.6 µg/g	Toxaphene-I (21 generations exp.); in acetone.	373
Periplaneta americana (adult ♂)	Injection	LD_{50} 96 hr.	25.0 µg/g	In xylene + acetone + ethanol + deobase 1:1:7.5:.5.	558
Periplaneta americana (adult ♀)	Injection	LD_{50} 96 hr.	80.0 µg/g	In " " " " " " " 1:1:7.5:.5.	558
Protoparce sexta (larva 5th instar)	Topical	LD_{50}	1363 µg/larva	5.4 (4.1-7.5)g av. wgt. larva.	1306
Protoparce sexta (larva 5th instar)	or	LD_{50}	143 µg/larva	" " " " " ".	1306
Protoparce sexta (larva 5th instar)	Topical	LD_{90}	5778 µg/larva	" " " " " ".	1306
Protoparce sexta (larva 5th instar)	or	LD_{90}	6025 µg/larva	" " " " " ".	1306
Protoparce sexta (larva 3rd,4th instar)	Topical	LD_{50}	32 µg/larva	2.5 (1.2-4.0)g av. wgt. larva.	1306
Protoparce sexta (larva 3rd,4th instar)	Topical	LD_{90}	138 µg/larva	" " " " " ".	1306
Protoparce sexta (larva 2nd,3rd instar)	Topical	LD_{50}	30 µg/larva	0.9 (0.6-1.1)g av. wgt. larva.	1306
Protoparce sexta (larva 2nd,3rd instar)	Topical	LD_{90}	112 µg/larva	" " " " " ".	1306
Oncopeltus fasciatus ♂♀	Dipping	LC_{50}	190 µg/cc	Laboratory Strain, unselected.	1258
Oncopeltus fasciatus ♂♀	Dipping	LC_{50}	345 µg/cc	17 generations of selection by toxaphene.	1258

b) Residual action of toxaphene vs. hornflies; insects exposed (at various intervals after treatment) to cages treated with 0.5% wettable powder emulsions: 353

Interval After Treatment Of Cage	Time (minutes) For 100% "Knockdown"
24 hrs.	73
3 weeks	172
2 months	248

(1) Comparative effectiveness toward Periplaneta americana of toxaphene and other compounds in urea-formaldehyde wall coatings; 50% insecticide based on dry weight of coating: 267

Insecticide	Time For 50% Knockdown (Hrs.)	Time For 100% Knockdown (Hrs.)
Toxaphene®	>48 hrs.	—
DDD	>48 hrs.	—
DDT	24 hrs.	48 hrs.
Chlordane	15 hrs.	18 hrs.
Lindane	1 hr.	1.5 hrs.

(2) Comparative effectiveness vs. Musca domestica of toxaphene and other compounds in various wall coatings containing 20% insecticide (dry wgt. basis) initially, and at various intervals after application to a surface: 267

Insecticide	Type Coating	Time For 50% Knockdown (Minutes)		
		Initially	After Interval Specified	Interval Between Tests (Weeks)
Toxaphene®	Urea-Formaldehyde	48	35	12
DDT	" "	16	10	28
Lindane	" "	13	16	6
Chlordane	" "	60	41	7
DDD	" "	28	25	17
Pyrethrum	" "	18	2,11,23,52 days	8,14,15,17 days
Toxaphene®	Nitrocellulose	55	26	12
DDT	"	60	17	35
Lindane	"	39	20	30
Chlordane	"	76	28	30

c) Comparative toxicity, toxaphene and other insecticides:

(1) Vs. Artemia salina (brine shrimp, Crustacea) used as a test organism for bioassay; insecticides in acetone solution: 2251

Insecticide	Time For Adults To Sink To Bottom Of Water Column Through Swimming Movement Failure At Indicated Concentration		
	1 ppm	0.1 ppm	0.01 ppm
Toxaphene®	45-60 min.	90-120 min.	18 hrs.
Chlordane	60-120 "	120-135 "	120-180 min.
Methoxychlor	45-60 "	45-60 "	45-60 "

(1) Vs. Artemia salina (brine shrimp, Crustacea) used as a test organism for bioassay; insecticides in acetone solution: (continued) 2251

Insecticide	Time For Adults To Sink To Bottom Of Water Column Through Swimming Movement Failure At Indicated Concentration		
	1 ppm	0.1 ppm	0.01 ppm
Lindane	45-60 min.	60-120 min.	60-120 min.
DDT	60 "	60 "	60-120 "
Acetone control 1 : 100		24 - 48 hours.	
Water "		26 - 50 hours.	

(2) Vs. Anopheles quadrimaculatus (4 day old adults) by topical application: 2051

Insecticide	LD$_{50}$ (μg/insect)		LD$_{90}$ (μg/insect)	
	♂	♀	♂	♀
Toxaphene®	0.15	0.29	0.29	0.5
p,p′-DDT	.02	.066	.045	.13
p,p′-DDD	.041	.1	.098	.22
Methoxychlor(tech.)	.035	.1	.078	.22
Chlordane	.105	.24	.19	.46
Dieldrin	.009	.023	.022	.048
Lindane	.0085	.011	.032	.042
Malathion	.0087	.0095	.019	.022
Allethrin	.0029	.008	.013	.041

Relative effectiveness (DDT = 1.0) At				
Insecticide	LD$_{50}$		LD$_{90}$	
	♂	♀	♂	♀
Toxaphene®	0.13	0.23	0.16	0.26
Chlordane	.19	.28	.24	.28
p,p′-DDD	.49	.66	.46	.59
Methoxychlor	.57	.66	.58	.59
p,p′-DDT	1.0	1.0	1.0	1.0
Dieldrin	2.2	2.9	2.0	2.7
Lindane	2.4	6.0	1.4	3.1
Allethrin	6.9	8.3	3.5	3.2
Malathion	2.3	7.0	2.4	5.9

(3) Vs. Anthonomus grandis; % active ingredient as lbs. per acre to give 50% mortality; combined oral and contact action; insects placed on dusted cotton plants: 2276

Insecticide	Lbs./Acre To Yield 50% Kill
Toxaphene®	6.4
Dieldrin	0.9
Aldrin	1.1
BHC (tech.)	1.0
Chlordane	10.1
DDT	9.1
Prolan (tech.)	11.4
Bulan (tech.)	16.7

(4) Vs. Apis mellifera (adult workers); as oral poisons given in 50% sugar solution: 1718

Insecticide	μg/Bee To Yield Mortality Shown In 24 Hrs.		
	20%	50%	90%
Toxaphene®	25.12	39.81	80.17
Parathion	.018	.040	.144
TEPP	.052	.065	.093
Lindane	.026	.079	.346
Dieldrin	.223	.269	.354
Aldrin	.181	.239	.365
Chlordane	.831	1.122	1.730
Systox®	1.256	1.478	1.884
Dimefox®	1.250	1.905	3.506

(5) Vs. Apis mellifera; as aqueous contact sprays; average deposit of 7.6 mg per cm^2 × 10^{-5} = 5.3 mg per bee × 10^{-5}: 1718

Insecticide	Amount As μg/cm^2 To Yield % Mortality Indicated		
	20%	50%	90%
Toxaphene®	36.73	44.67	59.98
Parathion	.257	.354	.574
TEPP	.358	.445	.621
Dieldrin	.386	.575	1.052
Aldrin	.327	.562	1.274
Lindane	.772	.851	.986
Chlordane	3.802	5.00	7.580
Systox®	4.321	5.123	6.619
Dimefox®	16.520	23.17	38.640

(6) Vs. Apis mellifera (adult workers) in contact for 1 hour with residual films (dry) deposited on filter paper from aqueous media: 1718

Insecticide	% Kill In 24 Hrs.	Dry Film ($\mu g/cm^2$)	Average Field Dose ($\mu g/cm^2$)	Ounces/Acre
Toxaphene®	9	110	16.8	24
"	0	40	—	—
Dieldrin	90	.09	1.4	2
"	10	.04	—	—
Aldrin	75	.09	1.4	2
"	0	.04	—	—
Lindane	100	.28	2.8	4
"	0	.074	—	—
Parathion	90	.54	1.4	2
"	10	.18	—	—
Chlordane	100	3.4	11.2	16
"	12	.9	—	—
Systox®	50	10	—	—
"	22	6.8	—	—
TEPP	8	.22	5.6	8
Dimefox®	0	50	—	—

(7) Vs. Apis mellifera (adult worker); fumigant toxicity; bees exposed for 1 hr. to films on paper; insects not in contact, save via vapors (if any): 1718

Insecticide	% Kill In 24 Hrs	Dry Film ($\mu g/cm^2$)
Toxaphene®	0	70
Dieldrin	100	.280
"	0	.074
Lindane	100	.44
"	0	.28
Aldrin	100	.74
"	0	.074
Parathion	100	5.0
"	0	2.8
Chlordane	100	3.7
"	0	.37
TEPP	0	5.5
Systox®	0	18.5
Dimefox®	0	74.0

(8) Vs. Chrysops discalis; by topical application to adult insects: 2707

Insecticide	LD_{50} (estimated) (μg/fly)	LD_{90}
Toxaphene®	180	480
Lindane	4	35
Endrin	9	80
DDT	20	250
Dieldrin	20	950
Methoxychlor	30	90
Aldrin	40	170
Heptachlor	40	200
EPN®	48	120
Isodrin	60	170
Chlordane	60	650
Bayer 22/190*	65	420
Diazinon	90	360
Bayer 21/199**	90	910
Q-137	120	400
Malathion	130	330

*Chlorthion®

**3-Chloro-4-methylumbelliferone O,O-diethyl thiophosphate.

(9) Vs. Cirphis unipuncta (larva): 3268

Insecticide	LD_{50}, Topical ($\mu g/g$)	Ratio To Parathion(=1.0)	LD_{50}, Oral ($\mu g/g$)	Ratio To Parathion	Ratio LD_{50} : LD_{99} Topical	Oral
Toxaphene®	56.2	15.2	34.1	13.6	4.7	2.9
Parathion*	3.7	1.0	2.5	1.0	3.4	8.5

(9) Vs. Cirphis unipuncta (larva): (continued) 3268

Insecticide	LD$_{50}$, Topical (μg/g)	Ratio To Parathion (=1.0)	LD$_{50}$, Oral (μg/g)	Ratio To Parathion	Ratio LD$_{50}$: LD$_{99}$ Topical	Ratio LD$_{50}$: LD$_{99}$ Oral
DDT	193	52.2	45.7	18.3	4.7	22.8
Chlordane	117.5	31.6	78.2	31.3	4.9	4.7
Lindane	28.1	7.6	27.9	11.2	3.2	5.1
Aldrin	19.8	5.4	11.4	4.6	3.7	24.7
Dilan	8.8	2.4	11.5	4.6	5.4	5.0
Dieldrin	8.3	2.2	4.6	1.8	3.1	3.8

*Yielded fastest kill followed (in order) by dilan, lindane and DDT.

(10) Vs. Heliothis zea and Heliothis virescens (250-450 mg body weight) 6th instar larvae; topical application in methyl ethyl ketone solution: 1124

Insecticide	LD$_{50}$ (μg/g) H. zea	LD$_{50}$ (μg/g) H. virescens
Toxaphene®	2000	18,000
DDD	3000	17,000
DDT	3000	6,500
Endrin	17	180
Malathion	130	160
Bayer L 13/59	30	60
Bayer 17147	40	54
Shell OS-2046	4.8	4.8

(11) Vs. Locusta migratoria migratorioides; topical application in tractor vaporizing oil 9 parts + cyclohexanone 1 part to young, virgin adults: 1585

Insecticide	LD$_{50}$ 96 Hrs. (μg/insect)	LD$_{50}$ 96 Hrs. (μg/g)	LD$_{95}$ (μg/insect)	LD$_{95}$ (μg/g)
Toxaphene®*	40.2 ± 2.88*	38.1	123.0 ± 16.9	116.0
Methyl parathion	0.94±0.1	.89	2.3 ± 0.52	2.2
Lindane	3.89± .21	3.69	12.9 ± 2.09	12.2
DNOC	10.4 ± .1	9.9	19.3 ± .897	18.3
Chlordane	20.4 ±1.05	19.3	110.0 ± 30.9	104.0
DDT	140.0 ± 7.6 **	133.0	258.0 ± 18.6	245.0

*In the original referred to as chlorinated camphene.
**LD$_{50}$ 5 days.

(12) Vs. Melanoplus differentialis; for topical application in dioxane, acetone, ethanol solutions; for oral administration as a deposit on leaves: 3267, 1102

Insecticide	Vs. Adult Insects (μg/g) LD$_{50}$, Topical	Vs. Adult Insects (μg/g) LD$_{50}$, Oral	Vs. 1st, 2nd Instar Nymphs, Field Tests Contact Spray, LD$_{50}$ As Lbs. Active Ingredient/Acre
Toxaphene®	61.0; 73.9	75.0; 91.5	0.91
DDT	>3300; 9380.0	>1350; 2579.0; 1170.0*	—
Chlordane	9.8; 16.3	12.0; 21.8	0.49
Lindane	1.6; 3.4	6.6; 6.7	0.08
BHC	—	—	0.04
Heptachlor	1.6; 2.6	4.4; 6.0	—
Aldrin	1.8	2.3	0.04
Dieldrin	1.4	3.7	0.03
Parathion (tech.)	0.7; 0.8	6.0; 8.9	0.05
TEPP	4.4	—	—
HETP	18.4	—	—

* As a colloidal suspension directly applied to mouth parts.

(13) Vs. Melolontha melolontha (an insect for which DDT is not efficacious;) by topical application: 3184

Insecticide	μg/insect LD$_{50}$ 5 day	μg/insect LD$_{80}$ 5 day	Relative Toxicity At LD$_{50}$	Relative Toxicity At LD$_{80}$
Toxaphene®	ca. 7	ca. 20	ca. 0.1	ca. 0.12
BHC (tech.)	0.7	2.5	1.0(standard)	1.0
Dieldrin	1.6	5.0	0.4	0.5
Aldrin	2.7	> 6.0	0.25	<0.4
Chlordane	9.0	20.0	0.08	0.12

(14) Vs. *Musca domestica* (adult) as contact sprays; applied by a turntable modification of the method of Peet-Grady; KD 10 min. = "knockdown" in 10 minutes: 2033

Insecticide	Concentration (mg/cc) To Yield 50% Mortality In 24 Hrs.	KD 10 minutes At LC_{50} 24 Hrs. (%)
Toxaphene®	0.68	0
Dieldrin	.017	0
Parathion	.02	0
Methylparathion	.025	0
Lindane	.046	0
Heptachlor	.052	0
Aldrin	.056	0
TEPP	.069	ca. 70
Chlordane	.25	0
DDT	.35	0
Malathion	.48	0
Tetrapropyl dithiopyrophosphate	.68	0
Dilan	.72	ca. 30
Isolan	1.15	100
Allethrin	1.5	100
Pyrolan	5.5	100

(15) Vs. *Musca domestica* (adults) of various DDT-R and DDT-non R biotypes; by the measured drop test, topical application: 78

Biotype	LD_{50} 24 Hours For						
	Toxaphene®	DDT	DDD	Methoxychlor	Lindane	Heptachlor	Pyrethrins
Bellflower (DDT-R)	0.6	10.0	20.0	1.0	0.08	0.06	1.0
San José (DDT-R)	0.4	0.7	—	0.3	0.05	0.07	2.0
Ontario (DDT-R)	0.5	0.5	—	0.3	0.05	0.07	2.0
Riverside (DDT-R)	0.5	0.5	—	0.3	0.06	0.07	2.0
Laboratory (DDT-non R)	0.2	0.02	0.1	0.07	0.01	0.03	1.0

(16) Vs. *Periplaneta americana* (adults) by injection application; insecticides dissolved in xylene + acetone + deobase + absolute ethanol at 10 to 10 to 75 to 5:

Insecticide	LD_{50} 96 Hour ($\mu g/g$)		Ratio $\frac{LD_{50}\,♀♀}{LD_{50}\,♂♂}$
	♂♂	♀♀	
Toxaphene®	25	80	3.2
Lindane	0.8	4.4	5.5
Dieldrin	1	5	5
DDT	4.5	20	4.4
Chlordane	26	52	2.0
Methoxychlor	7	18	2.5

(17) Vs. *Protoparce sexta* (larvae); L = large larvae, 5th instar, 5.4 (4.1-7.5) g weight; M = medium larvae, 3rd, 4th instar, 2.5 (1.2 - 4.0) g; S = small larvae, 2nd, 3rd instar, 0.9 (0.6-1.1) g: 1306

Insecticide	μg/larva											
	LD_{50} Topical			LD_{90} Topical			LD_{50}, Oral			LD_{90}, Oral		
	L	M	S	L	M	S	L	M	S	L	M	S
Toxaphene®	1363	32	30	5778	138	112	143	—	—	6025	—	—
Endrin	42	2.9	0.51	219	6.3	6.3	9.9	—	0.11	49	—	0.85
Parathion	52	9.9	2.8	183	64	12.3	15.7	—	—	54	—	—
Isodrin	87	7.6	3.0	490	29	56	15.3	—	1.1	138	—	3.1
Lindane	206	—	—	1235	—	—	209	—	—	398	—	—
Malathion	481	61	23.6	1276	553	92	365	—	—	1621	—	—
Dieldrin	482	—	—	2559	—	—	—	—	—	—	—	—
Aldrin	487	—	—	1359	—	—	—	—	—	—	—	—
Heptachlor	1058	—	—	4005	—	—	—	—	—	—	—	—
DDD	2622	376	37	9813	2620	367	878	—	22.5	3192	—	58
DDT	$\gg$4000	2334	336	—	9887	1342	4416	—	158	28040	—	1125

(18) Vs. *Musca domestica* (maggots); Laboratory tests (Field tests much less encouraging); as emulsions mixed with the rearing medium: 1326

Insecticide	% Mortality At mg Active Ingredient/K of Medium Indicated					
	50 mg	20 mg	15 mg	10 mg	5 mg	2 mg
Toxaphene®	100	100	—	100	75	0
DDT	100	—	—	—	—	—
Methoxychlor	25	—	—	—	—	—

(18) Vs. Musca domestica (maggots); Laboratory tests (Field tests much less encouraging); as emulsions mixed with the rearing medium: (continued) 1326

Insecticide	% Mortality At mg Active Ingredient/K Of Medium Indicated					
	50 mg	20 mg	15 mg	10 mg	5 mg	2 mg
Lindane	—	99.5	—	60	—	—
Chlordane	—	—	100	—	—	75
Aldrin	—	—	100	100	100	97.5
Dieldrin	—	100	—	100	100	94
Heptachlor	—	100	—	—	100	90
Dilan	99.5	100	—	100	5	—

(19) Vs. Sphenarium purpurascens on corn plants; field tests:

Insecticide	Concentration (%) Dust	Active Ingredient Lbs./Acre	% Mortality After	
			12 Hrs.	24 Hrs.
Toxaphene®	5	1.74	26.8 (18-36)	53 (46-60)
"	10	3.6	40.4 (36-47)	61.4 (55-69)
Dieldrin	1	.35	74.2 (68-80)	98.2 (96-100)
"	2.5	.88	89.8 (87-93)	99.8 (99-100)
Aldrin	1	.32	77.8 (69-88)	97.8 (95-100)
"	2.5	.82	88.6 (83-96)	99.6 (99-100)
BHC	1	.36	86.6 (78-92)	94.2 (90-97)
"	2.5	.85	93 (89-98)	97 (93-100)
Isodrin	0.5 (spray)	.43	83.2 (81-92)	91.4 (80-96)
Parathion	0.5	.16	43.6 (36-51)	69.4 (61-80)
"	1.0	.35	66.8 (59-80)	76 (69-84)
Chlordane	2.5	.95	32 (27-39)	46.6 (41-54)
"	5	1.8	49.6 (39-62)	63.8 (50-77)
Endrin	0.5 (spray)	.36	32.8 (24-40)	47.6 (43-59)

(20) Speed of toxic action vs. Macrosiphum pisi on Vicia faba; using dusts applied in a dusting tower method; talc diluent: 520

Insecticide	Concentration (%)	°F	Time For			
			50% Mortality		98% Mortality	
			Hrs.	Min.	Hrs.	Min.
Talc Control		67-72	13	28	23	51
Toxaphene®	5	72	13	20	19	1
Chlordane	5	72	0	24	18	8
EPN®	0.86	74	5	26	8	6
Dieldrin	1	75	4	7	6	43
Aldrin	1	75	3	44	7	32
DDD	5	72	2	34	4	35
Methoxychlor	10	75	2	1	5	34
Parathion	1	70	1	8	1	43
"	2	70	1	21	1	53
DDT	5	72	0	57	1	45
Lindane	1	72	0	56	1	54
Rotenone	5	72	0	47	1	23
TEPP	0.18	74	0	20	0	56
Nicotine	1	72	0	15	1	12
"	3	72	0	12	0	20

(21) Vs. Anasa tristis (adult); by topical application in acetone solution; laboratory tests: 3376

Insecticide	% Mortality At 72 hrs. At Dosages Indicated				
	32 μg/g	64 μg/g	128 μg/g	256 μg/g	512 μg/g
Toxaphene®	—	—	16.7	66.7	82
Parathion	100	100	100	100	100
Lindane	83.3	100	100	100	100
Aldrin	—	93.3	100	100	100
Endrin	—	—	100	100	100
EPN®	—	—	100	100	100
Heptachlor	—	83.3	90	100	100
Isodrin	—	—	90	100	100
Dieldrin	—	—	70	100	100
Chlordane	—	—	36.7	80	90
DDT	—	—	20	30	76.7

(22) Vs. Aëdes dorsalis, Aëdes vexans (larvae, pupae) in laboratory tests conducted at 75°F: 2283

Insecticide	Stage	% Mortality At			
		1 ppm	0.5 ppm	0.2 ppm	0.1 ppm
Toxaphene®	Larva	96	93	91	84
Aldrin	"	100	96.9	99	95
DDT	"	100	96.9	100	98
Dieldrin	"	100	96.9	99	95
Endrin	"	100	98.9	98	98
Isodrin	"	100	98	97	81
Toxaphene®	Pupae	—	2.3	2.7	—
Aldrin	"	—	30.4	34	—
DDT	"	—	30	8.2	—
Dieldrin	"	—	78	63	—
Endrin	"	—	99	61	—
Isodrin	"	—	70	58	—

d) Effects of toxaphene on beneficial insects:

(1) On the bee, Apis mellifera: Toxaphene® is stated to be the least hazardous of the mass insecticides for the honey bee and may be used with safety on nectar-bearing flowering plants. When applied as a dust to blooming alfalfa the mortality among the honey bee field force is less than 10%. For comparative data consult the section titled Bees and Insecticides in this work. 3099, 910 3098, 429

(2) Resurgences of pests after use of toxaphene: By its deleterious effects on certain natural insect enemies and predators, the use of toxaphene is reported to have led to resurgences of Tetranychus telarius and Macrosiphum pisi "populations". 2650

(3) Effect on enemies of and predators on harmful insects: Toxaphene® (like DDT, parathion, dieldrin, endrin, demeton) has a high to moderate toxicity for members of the following beneficial genera of insect predators: Orius, Geocoris, Nabis, Chrysopa and Hippodamia although the larvae of Chrysopa and Orius are relatively tolerant. 3171

(a) Use of toxaphene under various circumstances is reported to have had the following effect for beneficial predators: Complete elimination of Nabis ferus and Stethorus punctum, Tetracnemus pretiosus, mortalities of 50%-95% of Scymnus binaevatus, Coleomegilla maculata, Hippodamia convergens. 2650

(b) As dusts, vs. beneficial insects (adults), placed on plants previously vacuum dusted with the toxicants: 1404

Insecticide	Conc. %	% Mortality 24 Hrs. Of		
		Collops vittatus	Hippodamia convergens	Coleomegilla maculata
Toxaphene®	10	32	12	36
DDT	5	38	6	32
Perthane	5	23	6	12
Strobane®	5	10	18	12
Heptachlor	2.5	41	30	38
Endrin	1	27	10	18
Dieldrin	2	36	4	24
Parathion	2	65	78	98
Malathion	5	47	90	100
Chlorthion®	5	64	82	100
Diazinon	4	37	66	100
Control	—	11	4	0
Lowest Sig.Diff.5% level	—	20	24	26

(4) Used against cotton insects as a toxaphene + sulfur dust after 2 early season toxaphene + DDT sprays reported to yield the lowest "population" of injurious insects and the highest "population" of beneficial insects compared with other insecticides. 3293

e) Miscellaneous comments:

(1) A recent report states that an arsonated toxaphene is more effective than toxaphene proper vs. Anthonomus grandis (boll weevil) and it is pronounced the "most toxic of various tested organic arsenicals." 894

(2) In residual toxicity of dry insecticide film deposits on filter paper, toxaphene is reported to have for Sitophilus granarius (adults) at 120 hr. exposures a relative potency to DDT of 0.16 (0.12-0.21; 5% fiducial limits) whereas parathion has a relative potency with respect to DDT of 11.1 (6.0-29.7). Films were deposited in P31 oil on Whatman #1 filter papers. 2999

f) Pharmacological, pharmacodynamic, physiological, etc.; for insects:

(1) The mode of action of toxaphene in insects is but little known or understood. Data are extremely meager. 2231

(2) When applied to insects the neurotoxic symptoms manifest themselves only after a latent period. Applied to the leg of Periplaneta americana, toxaphene induced (after a 3 hour latent period) a continuous low frequency repetitive discharge as recorded from the crural nerve. 520

(3) Toxaphene® did not stimulate the motor nerves of isolated legs of Periplaneta americana or Calliphora erythrocephala. The presumption was drawn that toxaphene (like chlordane and unlike DDT) acts centrally at the ganglion and requires to reveal its action peripherally an intact reflex arc. 295

(4) Blattella germanica, having received by injection 100 μg of toxaphene, showed (after a 1 hour latent period during which the insect was passive) an increase in O_2 consumption reaching 3 times the normal levels. The upturn in O_2 uptake was associated with the onset of the phase of hyperactivity and the normal level was resumed with the oncoming of paralysis. 1441

(5) Toxaphene® is reported to exercise a slight disturbing and stimulating effect on the heart-beat of Periplaneta americana upon injection of 80 μg into either normal or beheaded subjects. The heart stopped in systole. 2421

(6) Toxaphene®, at 10^{-3} and 10^{-5} M concentrations, brought about a complete inhibition of cytochrome oxidase (from Periplaneta americana coxal muscle) in vitro systems as measured by O_2 uptake in Warburg's apparatus. The inhibition was of rapid onset and in the case of 10^{-5} M concentration followed a slight transient stimulation. 2305

(7) The insecticidal action of toxaphene has a high temperature coefficient. Mortality of treated insects is 1561
increased by high post-treatment and exposure temperatures, for instance Musca domestica showed a 1755
higher mortality when exposed continuously to residual deposits at 90°F than at 70°F.

(8) Ad hoc resistance to toxaphene has appeared in insects subjected to selection by exposure for many 1597,2231
generations. In addition certain biotypes of DDT-R Musca domestica reveal an enhanced tolerance 1258
for toxaphene.

g) Field reports on the effectiveness of toxaphene vs. economic insects:

(1) Vs. Haematopinus eurysternus on cattle as a spot treatment 0.5% concentrations yielded 100% mortalities in 24, 48 hours and remained effective during 4 weeks. 2862

(2) Vs. Eomenacanthus stramineus on chickens 5% dusts in kaolin yielded complete control of the original infestation and remained effective against reinfestation for 4 weeks. 2862

(3) Vs. Musca domestica at 1% concentration in sugar, molasses baits toxaphene in laboratory tests showed 40% mortality or "knockdown" in 30 minutes, 56% in 1 hour, 100% in 24 hours but proved unsatisfactory to control in the field. 1915

(4) Vs. Pieris rapae and Trichoplusia ni: Yielded 80.8% control as a 37.3% dust of infestations in which T. ni was predominant. 796

(5) Vs. grasshoppers:

(a) While of less toxicity than chlordane proved not greatly inferior to chlordane in field. 3266

(b) Melanoplus: 95% control at 2 lbs./acre (chlordane gave 98% control). 2028

(c) Yielded at 1.5 lbs. per acre (spray) same control as chlordane at 1 lb. per acre; as a dust at 2 lbs. per acre yielded same control as chlordane at 1.5 lbs. per acre. 2446

(d) Recommended as a wettable powder at 1.5 lbs. per acre in presence of enough edible vegetation; for young nymphs 1 lb. per acre sufficed. 1373,2555

(e) Kills slowly, largely as a stomach poison, in case of Melanoplus. 330,1100

(f) At 4% in baits at ca. 5 lbs. per acre gave 70% control of Melanoplus mexicanus. 354

(6) Vs. Nezara, Murgantia: Equal to DDT in the control yielded. 1099,2882

(7) Vs. Euschistus tristigmus: Effective but less so than sabadilla. 3368

(8) Vs. Psallus seriatus: 10% toxaphene effective; yielded control equal to DDT. 2438

(9) Vs. Philaenus leucophthalmus: Superior to DDT, BHC, chlordane at 1.5 lbs. per acre level. 512

(10) Vs. Empoasca fabae: Equal to DDT in control of. 2450

(11) Vs. Psylla pyricola: Decisive control with persistence equal to rotenone; superior to DDT, BHC, chlordane, HETP. 1359

(12) Vs. Aphis gossypii: Effective in control of severe infestations. 91

(13) Vs. Pseudococcus comstocki: Incomplete control. 2356

(14) Vs. Heliothrips haemorrhoidalis: Less toxic than DDT. 2227

(15) Vs. Frankliniella tritici: Yielded control on cotton. 1096

(16) Vs. Thrips tabaci: As 5% dusts much superior to DDT. 995

(17) Vs. Protoparce sexta, P. quinquemaculata: 10% dusts more effective than cryolite or DDT. 821

(18) Vs. Malacosoma americanum: Equal to DDT in yielding 100% control with 0.1% suspension sprays. 2960

(19) Vs. Anticarsia gemmatilis: Much superior to cryolite in control of. 110

(20) Vs. Alabama argillacea: Yielded effective control of. 91

(21) Vs. Cirphis unipuncta, Prodenia eridania, Laphygma frugiperda: Inferior (as dust) to DDT, DDD. 1572

(22) Vs. Agrotis orthogonia: Less effective than chlordane, pyrethrins, DNOC or lindane. 350

(23) Vs. Heliothis armigera: Less effective (as dusts) than DDT on corn or tomatoes. 1874

(24) Vs. Cotton Bollworm: Yielded control with 20% dusts at 10-15 lbs. per acre. 91

(25) Vs. Argyrotaenia velutinana: 0.1% spray yielded fair-good control. 1199,1235

(26) Vs. Polychrosis viteana: Ineffective. 624

(27) Vs. Carpocapsa pomonella: Ineffective in control of. 3263

(28) Vs. Loxostege similalis: As 20% dust superior to DDT 10% dust on cotton. 91

(29) Vs. Thyridopteryx ephemeraeformis: 0.2% sprays yielded 92% control. 951

(30) Vs. Hylemya brassicae; H. cilicrura: Ineffective as a soil insecticide. 659,1034

(31) Vs. Monarthropalpus buxi: 0.2% sprays gave 100% kills in mined foliage. 2960

(32) Vs. Epilachna varivestis: Slightly more effective than DDT. 2959

(33) Vs. Popillia japonica: Effective but not as effective as chlordane. 2776

(34) Vs. Cotinis nitida: Less effective than parathion. 822

(35) Vs. Leptinotarsa decemlineata: As 0.1% sprays equal in effect to DDT in the field. 2279

(36) Vs. Epitrix cucumeris: Slightly less effective than DDT. 3142

(37) Vs. Epitrix hirtipennis: 90-95% control yielded by sprays of. 820

(38) Vs. *Diabrotica duodecempunctata*: 10% dusts in area treatment gave 80% control. 1876

(39) Vs. *Dendroctonus monticolae*: Less effective than BHC. 1854

(40) Vs. *Chalcodermus aeneus*: More effective than DDT, BHC or chlordane. 3280

(41) Vs. *Brachyrhinus ligustici*: As a dust greatly more effective than sodium fluosilicate. 1312

(42) Vs. *Anthonomus grandis*: Moderately effective. Recommended at 2 lbs. per acre in dusts (20 lbs. per acre as 10% formulation). Better, faster control than with aldrin, BHC, DDT, dieldrin when not subjected to rain. 91,74 2585

(43) Vs. *Anthonomus signatus*: Less effective than DDT. 2143

(44) Vs. *Conotrachelus nenuphar*: Effective, but phytotoxic to peach tree foliage. 2915

(45) Vs. Orchard Mites: Good control reported for some, using toxaphene. 2369,2705

(46) Vs. *Tetranychus bimaculatus*: Yielded control of. 1619

(47) Vs. *Amblyomma americana*: Area sprays at 2 lbs. per acre gave effective control for 2 months. 2167

(48) Vs. *Blattella germanica*: Superior to DDT. 2451

(49) Vs. *Wasmannia auropunctata*: Effective control with toxaphene. 2422

(50) Vs. *Cimex lectularius*: Less toxic and effective than DDT as a residual spray but more toxic than DDT by direct contact. 2451

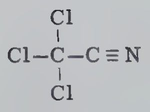
(51) Vs. *Musca domestica*: As a spray in dairy barns gave effective control. Allows rapid reinfestation. 2319, 79

(52) Vs. *Siphona exigua*: Sprays protected cattle as well as DDT. 353

(53) Vs. *Hypoderma bovis*: Inferior to others in control of. 3066

184

TRICHLOROACETONITRILE (Tritox [I.G. Farben industrie])



$$\mathrm{Cl{-}\overset{\displaystyle Cl}{\underset{\displaystyle Cl}{C}}{-}C{\equiv}N}$$

Molecular weight 144.399

GENERAL (Also consult Acrylonitrile.) [Refs.: 2486, 616, 1197, 353, 2815, 1059, 757, 312]

An insecticidal fumigant which in spite of a rather high boiling point (85°C) is readily vaporized. The maximum concentration of vapor attainable at 25°C is 20 times the concentration needed for practical fumigation. Absorption of trichloroacetonitrile by various materials is low; houses may be occupied again a few hours following treatment. The vapors are non-inflammable and there is no effect on metals, polishes, paints, silks and dried fruits nor on iron or steel, except at high humidities. The vapors are toxic to man and animals but are intensely lachrymatory and thus self-warning, at very low concentration, presenting little hazard if exit or escape are possible. Less toxic to man than acrylonitrile but intensely irritating at 5 - 10 mg per m^3. The toxicity for man is comparable to that of ethylene oxide, q.v. May, under certain conditions, unless directions are carefully followed, give rise to phosgene. Extensively used in Germany as a louse and bed bug fumigant. Useful at 2 lbs per 1000 ft^3 in the fumigation of stored products. Effective at 1.5 lbs per 1000 bushels in the fumigation of stored grains. 30 g per m^3 is a fatal concentration for many insects in 8 hour exposures at 20°C. Moths require a higher concentration. As a 1:1 mixture, trichloroacetonitrile + acrylonitrile has proved effective as a penetrating house fumigant, soon dissipated by ventilation. Compares favorably with ethylene oxide as a fumigant for binned grain; no trace remains after 48 hrs. ventilation.

PHYSICAL, CHEMICAL

A colorless to yellow liquid; freezing point -42°C; b.p. ca. 85°C; $d_{4°}^{25°}$ (liquid) 1.44; specific gravity of vapor (air = 1) = 4.95; not flammable; slightly soluble in water; soluble in some organic solvents; intensely irritating and lachrymatory at 5 - 10 mg/m^3; somewhat corrosive to iron at high humidity; hydrolyzed by alkali; saturation concentration (vapor) at 25°C, ca. 760 mmHg = 600 mg/l; 1 mg/l = 170.3 ppm; 1 ppm = 0.00589 mg/l.

1) Formulations: As such, stabilized with 2% Na_2CO_3 by weight and saturated with SO_2.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) No quantitative data were available to this compilation at the time of writing.
   b) Less toxic than acrylonitrile to man. Mice tolerated trichloroacetonitrile at doses higher than SO_2, thus as much as 2.9 g/m^3 were tolerated, whereas SO_2 was fatal at 2.76 g/m^3. 2486 1991

2) Phytotoxicity:
   a) At 3 lbs/1000 ft^3 gave no effect on the germination capacity of seed wheat. 468
   b) In tests vs. White Victor wheat: Fumigated at 20°C, 24 - 48 hours exposure, the effect on germination capacity was not severe. Exposure to 4 lbs/1000 ft^3 for 24 hours delayed germination slightly, 48 hours exposure reduced germination from ca. 80% to ca. 60%. 312
      (1) No effect on vitamin B complex in White Victor or Marquis wheats exposed at 20°C for 48 hours to 72 mg/l (4.5 lbs/1000 ft^3).
      (2) Phytotoxic for lemon fruits fumigated for Aonidiella aurantii.
   c) Toxicity toward growing plants: Potted plants fumigated by Aerograph gun at 15 lbs/in^2 (pressure), exposure 1 hour at 15° - 20°C. 5 mg/l kills lettuce, severely scorches Chrysanthemum, tomato, slightly scorches Vicia faba, Primula spp., Cineraria varieties. 312

3) Toxicity for insects:
   a) As effective as ethylene oxide in fumigation of dried fruits to control Oryzaephilus surinamensis and in fumigation of wheat vs. Sitophilus granarius. 312
   b) Less toxic than HCN, more toxic than methyl bromide vs. Aonidiella aurantii on lemon fruits. 312
   c) Slightly less toxic than acrylonitrile and chloroacetonitrile vs. Cimex lectularius. 2622
   c) Addition of CO_2 at 10% or over (v/v) enhanced the toxicity of trichloroacetonitrile vs. Sitophilus granarius, Tribolium castaneum, Ephestia kühniella and Cimex lectularius. 312
      (1) Toxicity to 4 insect pests, as average % mortality, in 5 hour exposures at 20°C; dessicator fumigation; mortality counts taken 7 days following exposure: 312

Concentration (mg/l)	Average % Mortality Of			
	Sitophilus granarius	Tribolium castaneum	Ephestia kühniella (larva)	Cimex lectularius
39.1	100	100	100	100
22.2	100	100	100	100

(1) Toxicity to 4 insect pests, as average % mortality, in 5 hour exposures at 20°C; dessicator fumigation; mortality counts taken 7 days following exposure (Continued): 312

Concentration (mg/l)	Average % Mortality Of *Sitophilus granarius*	*Tribolium castaneum*	*Ephestia kühniella* (larva)	*Cimex lectularius*
15.7	30	100	100	100
8.0	90	69	100	100
5.8	7	34	100	59
3.3	18	8	91	11
1.2	0	0	0	0
Control	0	1	10	10
HCN LC$_{50}$ mg/l—	10.2	0.19	0.13	0.11
HCN LC$_{99}$ mg/l—	28.3	0.54	0.33	0.33
Ethylene oxide LC$_{50}$ mg/l—	6.7	10.6	5.4	-
Ethylene oxide LC$_{99}$ mg/l—	13.3	35.4	19.1	-

(2) Toxicity vs. several insect forms exposed under the same conditions as given in the preceding tabulation: 312

Insect	Control Mortality (0 mg/l)	Average % Mortality Obtained At 5 mg/l	15 mg/l	25 mg/l
Sitodrepa panicea	7	92	-	-
Sitophilus oryzae	0	44	99	98
Sitophilus granarius	2	11	23	70
Ptinus tectus	8	59	100	100
Tenebrio molitor (larva)	0	15	98	97
Tineola biselliella (larva)	0	13	100	100
Trogoderma versicolor (larva)	2	16	15	50
Anthrenoceros australasiae (larva)	3	32	98	100

(3) Toxicity vs. *Musca domestica*; as a space spray applied by Aerograph gun at 15 lbs pressure per in.^{2} : 312

Concentration (mg/l)	Exposure (Hrs)	"Knockdown" (%)	Mortality (%)	Flies Liberated Immediately-
8.6	1	100	100	After spray
6.4	1	100	100	Before spray
4.3	1	99	92	After spray
4.3	1	100	56	After spray
3.5	2	100	100	Before spray
2.2	2	46	6	Before spray
3.2	3	-	56	Before spray
2.2	3	43	17	Before spray

(4) Toxicity of trichloroacetonitrile + various amounts of CO_2 vs. several insect species; conditions as in the preceding tabulation: 312

% CO_2 (v/v)	Trichloroacetonitrile (mg/l)	Average % Mortality Of *Sitophilus granarius*	*Tribolium castaneum*	*Ephestia kühniella*	*Cimex lectularius*
80	5	97	100	97	100
20	5	18	100	99	100
13	5	19	98	100	100
7.5	5	34	70	91	100
5.0	5	18	85	100	94
2.5	5	8	76	100	58
0	5	6	40	95	32
80	0	1	3	6	10

(5) Vs. *Aonidiella aurantii*, HCN-R biotypes: 403

Mortality (%) At 12 mg/l, 40 Min. Exp. At 59°F	 68°F	 77°F	 6 mg/l At 79°F	 12 mg/l At 82°F	 20 mg/l At 91°F	 Exp. 40 Min. At 77°F At 7.0 mg/l	 9.0 mg/l	 10.5 mg/l	 12.0 mg/l
90.8 ± 1.6	97.0 ±1.5	99.2 ± 0.4	22.8	96.5	99.8	46.3	78.3	84.8	92.5

Relative effectiveness: HCN > Trichloroacetonitrile > Methyl bromide.

(6) Trichloroacetonitrile in chamber fumigation vs. three household insect species; chamber furnished and equipped as a typical bedroom; fumigation at 1 lb/100 ft^3; chamber 740 ft^3; temperature: 75° - 85°F = high, 55° - 60°F = cool; Relative Humidity < 20% = dry, ca. 100% = damp: 1197

Exposure (Hrs)	°F	Moisture	% Mortality Of			Hours Needed for Aeration Of		
			Bedbug	Carpet Beetle (larva)	Flour Beetle	Sideboard	Mattress	Pillow
6	75°-85°	Dry	100	90	100	4	4	7
6	75°-85°	Damp	100	100	100	6	6	12
6	55°-60°	Dry	94	70	82	2	2	4
6	55°-60°	Damp	88	65	78	-	-	-
12	75°-85°	Dry	100	100	100	2	4	5
12	75°-85°	Damp	100	100	100	1	6	13
12	55°-60°	Dry	100	84	100	3	5	7
12	55°-60°	Damp	100	100	100	6	6	9
			Trichloroacetonitrile + Acrylonitrile 1:1					
6	75°-85°	Dry	96	84	94	2	2	5
6	75°-85°	Damp	100	95	100	4	5	10
6	55°-60°	Dry	94	50	98	-	-	-
6	55°-60°	Damp	100	20	78	-	-	-
12	75°-85°	Dry	100	100	100	2	2	6
12	75°-85°	Damp	100	100	100	5	5	8
12	55°-60°	Dry	100	75	100	6	6	8
12	55°-60°	Damp	100	90	-	6	7	13

(7) Vs. Lasioderma serricorne (larva) in baled Turkish tobacco; larvae exposed at various depths in bales: 181

Dosage Oz./1000 ft^3	Exposure (Hrs)	°F	% Mortality At Depth In Inches Shown					
			1 in.	2 in.	5 in.	7 in.	9 in.	Control
16	72	76	94.4	60.4	45.6	45.2	44.4	12.8
20	72	75.7	95.2	79.6	79.6	80.8	80.0	11.2
24	72	69.3	100	99.2	98.4	98.8	94.4	4.8
28	72	73.8	100	100	100	99.6	99.6	16.8
32	72	69.3	100	100	100	100	100	9.6

(8) Vs. Cimex lectularius under various conditions; exposure 5 hrs at 760 mmHg, 77°F; O = older nymphs, A = adults, E = eggs: 2622

Fumigant	% Mortality Wrapped								
	In Cotton Batting			In Woolen Blanket			Woolen Blanket In Barracks Bag		
	O	A	E	O	A	E	O	A	E
Trichloroacetonitrile	94.5	97.5	96.8	75	100	100	64	89.4	98.3
Methyl bromide	100	100	100	100	100	100	100	100	100
Chloropicrin	100	100	100	100	100	100	100	100	100
HCN	100	100	100	100	100	100	61.3	96.7	100
Acrylonitrile + CCl_4 1:1	100	100	100	92.8	100	100	20	25	20.5
1,1-Dichloro-1-nitroethane	76.6	97.5	78	66.7	97.9	84.3	31.5	67.4	54.3
Ethylene oxide	37.7	--	--	17.8	--	--	24.2	--	--
Chloroacetonitrile	30.6	75	--	1.9	7.3	--	14.8	14	--

(9) Vs. Cimex lectularius; by empty 12 liter flask fumigation, exposure 5 hours at 25°C:

Fumigant	Approximate LC_{95} - LC_{100} (mg/l) For		
	Older Nymphs	Adults	Eggs
Trichloroacetonitrile	11	8	< 8
Dichloroacetonitrile	10	< 8	< 8
Chloroacetonitrile (Mono-)	3 - 4	< 3	< 3
HCN	0.4	< 0.4	< 0.4
Acrylonitrile	3 - 4	< 2.5	2
Chloropicrin	5 - 6	3	< 2.75
α,β-Dichloroethyl ether	5 - 6	5 - 6	> 6
Acrylonitrile + CCl_4 1:1	7.5	6 - 7.5	6
1,1-Dichloro-1-nitroethane	8	< 8	< 8
Methyl bromide	9	< 7	< 7
Ethylene oxide	14	6 - 10	< 2
Methylallyl chloride	25 - 30	< 25	< 25
Ethyl formate	30	25 - 30	< 25
Ethylene oxide + ethylene Cl_2 1:3	35	25 - 30	< 25
Sym.-Tetrachloroethane	35	35	25
Carbon disulfide	37.5	< 30	30
Ethylene dichloride	> 50	> 50	> 50

(9) Vs. Cimex lectularius; by empty 12 liter flask fumigation, exposure 5 hours at 25°C (Continued):

Fumigant	Approximate LC_{95} - LC_{100} (mg/l) For		
	Older Nymphs	Adults	Eggs
Ethylene Cl_2 + CCl_4 3:1	>50	>50	>50
Carbon tetrachloride	"	"	"
Trichloroethylene	"	"	"

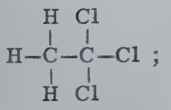
(10) Vs. Sitophilus oryzae and Tribolium confusum as a mixture trichloroacetonitrile 1: CCl_4 19 exposed at 72°F for 24 hrs: 616 2629

Insect	MLC (mg/l)		Conditions
	Mixture	Nitrile	
S. oryzae	47	2	Empty 20 liter flask fumigation.
"	396	ca. 16	Flask filled with wheat grain.
T. confusum	95	-	"

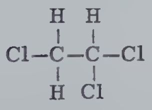
The mixture may be used at 35 lb/1000 bushels (1.5 lb/1000 bushels, nitrile) for S. oryzae; for T. confusum 8.4 lbs mixture/1000 bushels (0.38 lb nitrile/1000 bushels). T. confusum proved more susceptible than S. oryzae. Monochloroacetonitrile is slightly more toxic than acrylonitrile for T. confusum but a high b.p. (127°C) makes generation of vapor and its later elimination difficult.

185

TRICHLOROETHANE (1, 1, 1-Trichloroethane; Methyl chloroform) [with some consideration of 1, 1, 2-Trichloroethane (Vinyl trichloride)]


$H-\overset{H}{\underset{H}{C}}-\overset{Cl}{\underset{Cl}{C}}-Cl$;

1,1,1-trichloroethane


$Cl-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{Cl}{C}}-Cl$

1,1,2-trichloroethane

Molecular weight 133.42

GENERAL (N.B. DDT is a substituted 1,1,1-trichloroethane) [Refs.: 1801, 355, 1798, 353, 2815, 255, 984, 2670, 2603]

A substance which has been proposed for use and tested as a fumigant insecticide. Trichloroethane appears to act as a direct neurotoxicant in insects producing cytolysis in the insect nerve cord. Trichloroethane exists in the form of two isomers.

PHYSICAL, CHEMICAL

A colorless liquid; freezing point -32.7°C; b.p. 74.1°C; $d_{4°}^{20°}$ 1.349, $d_{4°}^{15°}$ 1.346; $n_D^{20°}$ 1.438; v.p. 120 mmHg at 25°C; insoluble in water; miscible with alcohol, ether; soluble in many organic solvents; not flammable; used as a solvent. 1,1,2-trichloroethane: Colorless liquid; freezing point -36.7°C; b.p. 113.5°C; $d_{4°}^{25.5°}$ 1.441; soluble to 0.44 part in 100 parts water at 20°C; miscible with alcohol, ether, chloroform; soluble in many organic solvents; used as a solvent.

TOXICOLOGICAL (1,1,1-trichloroethane)

1) Toxicity for higher animals:
   a) Readily absorbed via the lungs on inhalation.
      (1) Anaesthetic to frogs, rabbits and dogs with a rapid action and little effect on heart and respiratory rates. 3061
      (2) 20 grams by inhalation narcotize a man without producing excitement or marked alterations in respiration or pulse; recovery from narcosis is prompt. 3061
      (3) The minimum narcotic concentration for mice in 2 hour exposures is 45 mg per liter of air (0.00034 M per l). 1938
   b) Threshold Concentration, Continuous Exposure = 500 ppm. 56

c) Quantitative:

Animal	Route	Dose	Dosage	Remarks	
Mouse	inh	MLC	65 mg/l; 11,000 ppm	2 hours exposure.	1938
Rat*	inh	MLC	97.9 mg/l; 18,000 ppm	3 hours exposure.	10
Rat*	inh	MLC	82 mg/l; 14,500 ppm	7 hours exposure.	

*Death from cardiac or respiratory failure.

(1) Exposure of rats to graded dosages: 10

At 5000 ppm: Mild narcosis after 1 hour's exposure.

At 10,000 ppm: Increase in respiratory rate and amplitude (transient); in 10 minutes: Staggering; after 3 hours: Ear pallor, cold body, irregular respiration, semiconscious state; death, of heart and respiratory depression. Survivors completely recovered on day following exposure.

At 15,000 ppm: Effects as with 10,000 ppm but with more rapid onset.

At 18,000 ppm: All subjects helpless in 5 minutes; unconscious after 1 hour and after emergence from narcosis pale, cold and in semi-stupor; survivors showed quick recovery.

Monkeys at 5000 ppm: Some ataxia after 1 hour exposure; trembling of hands and forearms after 5 hours exposure; subjects normal after recovery in fresh air.

d) Repeated exposures:

(1) Guinea pigs at 5000 ppm, 7 hrs per day, 32 exposure periods in 45 days: Weight loss during first 21 days (later slowly regained); slight to moderate fatty liver degeneration; no necrosis or renal damage; some testicular degeneration in ♂ subjects. Similarly treated ♀ rats showed initial slight growth retard; no other effects. Rabbits exposed as above: No overt ill effects. 10

c) Pathology:

(1) Exposure to 18,000 ppm, 2 hours, rats: No significant visceral pathology on experimental killing 24 hours after exposure. 7 hours exposure at 12,000 ppm: Slight to moderate liver damage (vacuolation, congestion, necrosis in lobule centers, no kidney damage. At 8000 ppm, 7 hours exposure changes as above, but less severe. At 8000 ppm for 5 hours or 18,000 ppm for 30 minutes no pathological changes noted. 10

f) 1,1,2-Trichloroethane

(1) Absorption via lung, unbroken skin and gastro-intestinal system. 193,2788

(2) Action: Narcotic. Anaesthetizes frogs, Guinea pigs, dogs and pigeons without marked alteration in 397,195
pulse rate, respiratory rate or blood pressure. 3061

(3) Minimum narcotic concentration for mice in 2 hour exposures =15 mg/l (0.00011 M/liter). 3.3 times 1938
more active than chloroform in narcotizing action for cats. 1963

(4) Quantitative:

Animal	Route	Dose	Dosage	Remarks	
Rabbit	sc	MLD	500 mg/k	In oil; death in 24 hours.	195
Dog	or	MLD	750 mg/k	"	195
Dog	iv	MLD	95 mg/k	" ; death in 30 minutes.	195
Dog	or	MLD	0.5 cc/k		3378
Mouse	inh	LC	60 mg/l; 0.00045 M/l	2 hrs exposure; death within 24 hrs.	1938

(5) Animals undergoing 1,1,2-trichloroethane narcosis showed initial eye, nose and conjunctival irritation; tendon and corneal reflexes were the first lost; death occurred in respiratory arrest in the case of fatal dosages.

2) Toxicity for insects: (Also consult the general treatment titled, Fumigants.)

a) Reported to induce cytolysis (with opacity and shrinkage) of the insect central nerve cord. 2600

b) Quantitative:

1,1,1-trichloroethane:

Insect	Route	Dose	Dosage	Remarks	
Sitophilus oryzae (adult)	Fumig.	MLC_{100}	404 mg/l	Isomer unspecified; 24 hrs exp., ca. 25°C in 500 cc flasks with ca. 250 cc wheat.	2670
Dacus dorsalis (naked eggs)	Fumig.	LC_{50}	28 mg/l	2 hrs exposure, 71°-80°F, empty vessel.	255
Dacus dorsalis (")	Fumig.	LC_{95}	69 mg/l	" " "	255
Dacus dorsalis (larva)	Fumig.	LC_{50}	< 139 mg/l	" " "	255
Sitophilus granarius (adult)	Fumig.	LC_{50}	290 mg/l	5 hrs exposure, 25°C, empty flask.	984
Tribolium confusum (adult)	Fumig.	LC_{50}	66 mg/l	" " "	355

1,1,2-trichloroethane:

Insect	Route	Dose	Dosage	Remarks	
Tribolium confusum (adult)	Fumig.	LC_{50}	38.5 mg/l	5 hrs exposure, 25°C, empty flask.	156,2816
Tribolium confusum (adult)	Fumig.	LC_{99}	60.5 mg/l	" " "	156,2816
Sitophilus granarius (adult)	Fumig.	LC_{50}	53 mg/l	" " "	984
Tenebrioides mauritanicus (adult)	Fumig.	LC_{50}	0.352 cc/5 lbs; 0.508 g/5 lbs	24 hrs exp., 30°C, in 5 lb lots of shelled corn.	2603
Tenebrioides mauritanicus (adult)	Fumig.	LC_{95}	0.566 cc/5 lbs; 0.817 g/5 lbs	24 hrs exp., 30°C, in 5 lb lots of shelled corn.	2603

b) Quantitative:

trichloromethane (chloroform):

Insect	Route	Dose	Dosage	Remarks	
Tribolium confusum	Fumig	LC_{50}	157 mg/l	5 hrs exposure, 25°C, empty flask.	156,2816 1798
Tribolium confusum	Fumig	LC_{99}	267 mg/l	" " "	156,2816
Sitophilus granarius	Fumig	LC_{50}	240 mg/l	" " "	156,2816
Sitophilus granarius	Fumig	LC_{50}	250 mg/l	" " "	984
Sitophilus granarius	Fumig	LC_{99}	660 mg/l	" " "	156,2816

c) Comparative toxicity:

(1) Vs. Tenebrioides mauritanicus (adult); exposed for 34 hrs at 30°C in 5 lb lots of shelled corn: 2603

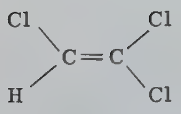
Fumigant	LC_{50}		LC_{95}	
	cc/5 lbs	g/5 lbs	cc/5 lbs	g/5 lbs
1,1,2-Trichloroethane	0.352	0.508	0.566	0.817
1,1-Dichloro-1-nitroethane	0.019	.027	.024	.034
Ethylene dibromide	.2	.043	.036	.078
Carbon disulfide	.102	.129	.111	.104
Methyl bromide + CCl_4 1:9	.120	.191	.161	.256
β-Methyl allyl chloride	.131;.108	.121;.100	.208;.191	.192;.177
Carbon tetrachloride	.276	.438	.455	.723
Ethylene dichloride	.467	.585	.903	1.135

(2) Vs. eggs and 3rd instar larvae of Dacus dorsalis; exposed for 2 hrs at 71°-80°F, in empty vessel: 255

Fumigant	Eggs		Larvae	
	LD_{50} — (mg/l) —	LD_{95}	LD_{50} — (mg/l) —	LD_{95}
1,1,1-Trichloroethane	28	69	<139	-
Acetonitrile	44	75	>82.4	
Chloroacetonitrile	1.2	1.5	<1.3	<1.3
Acrylonitrile	1.2	1.6	<1.2	1.6
Acrylonitrile + CCl_4 1:1	3.7	11	1.7	4.9
Carbon disulfide	53	92	56	89
Carbon tetrachloride	>167.8	-	>167.8	-
Methyl iodide	<2.9	<2.9	<2.9	4.2
Methyl thiocyanate	2.7	8.5	<1.4	<1.4
1-Bromo-2-chloroethane	<2.2	<2.2	<2.2	2.3
Ethylene dibromide	<2.9	<2.9	<2.9	<2.9
Chlorobromopropene	5.9	8.7	2.0	3.1
1,3-Dichloropropene	3.9	8.7	6.0	13.5
Ethyl chloroacetate	6.2	13.5	1.4	3.6
Methyl bromide	15.0	24.5	9.2	18.5
Methyl formate	65	110	-	-
Hydrogen cyanide	10	26	1.3	2.8
Propylene oxide	>89.4	-	18.5	28.0
Ethylene oxide	6.2	12.0	8.7	17.0
Ethylene dichloride	2.3	5.9	38	120
Ethyl formate	>104	-	-	-
Sym-Tetra chloroethane	25	68	20	43
1,1-Dichloro-1-nitroethane	24	60	<1.9	<1.9
Allyl chloride	71	105	70	>98.6
Allyl bromide	15	24	1.8	7.5

186

TRICHLOROETHYLENE (Ethylene trichloride; Ethinyl trichloride; Benzinol, Blacosolv; Cecolene; Chlorylen; Circosolv; Fleck-Flip; Lanadin; Lethurin; Perm-A-Chlor; Petzinol; Trethylene; Trial; Triclene; Tri-Clene; Trielin; Trilene; Westrosol; Vestrol; Vitran; Gemalgene; Germalgene; Tri; Triline; Trielene.)



Molecular weight 131.4

GENERAL (Also consult Tetrachloroethylene and Fumigants) [Refs.: 3199, 851, 2815, 2816, 353, 1059, 757, 156, 416, 3378]

An insecticidal fumigant which has been tested against various stored products and other insects. Trichloroethylene is also extensively used in fire extinguishers and as a solvent for oils, fats, waxes, greases, gums, tars and resins in dry-cleaning and to some extent as a general anaesthetic. Has anthelmintic properties.

PHYSICAL, CHEMICAL [Refs.: 2221, 3199, 851, 2671, 3013]

A colorless, mobile liquid; freezing point -73°C; b.p. 87.2°C; $d_{4°}^{20°}$ 1.4695; $n_D^{25°}$ 1.4556; v.p. 73 mmHg at 25°C; virtually insoluble in water (0.1 g/100 g at 25°C); miscible with some organic solvents such as alcohol, ether, chloroform; not flammable; chloroform-like odor; may be decomposed by heat with production of phosgene and HCl; vapor saturation at 25°C = 512 mg/liter; maximum amounts which can exist in vapor form in 1000 ft^3 at various temperatures:

°F	V.P. (mmHg)	Lbs As Vapor/1000 ft^3
32	23	11
59	44	20
68	57	25
77	73	32
86	94	41
95	119	51
104	149	63
113	185	76
122	224	91 ;

sorption by patent flour after 5 hours surface exposure at 25°C to 200 mg/l at 760 mmHg = 25.6 mg; sorption ratio in patent flour (CS_2 = 1) = 2.3; penetration through 3 inches patent flour after 24 hours exposure to 200 mg/l under standard conditions = 95.8 mg passed through in 24 hours; penetration ratio (CS_2 = 1) = 0.62; bulk density: 1 U.S. gallon = 12.1 lbs.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Less toxic to man than CCl_4. Long term toxicity greater than for CCl_4. 284 cases of poisoning in man gave 26 fatalities. 1665 1356

Animal	Route	Dose	Dosage (mg/k)	Remarks	
Animals	or	LD	3 - 4 cc/k	Death within a few hours.	772
Rabbit	or	LD	7330		1903
Rabbit	sc	MLD	1800	In oil; death in 24 hours.	195
Cat	or	LD	5864		1903
Dog	or	LD	5864		1903
Dog	iv	MLD	150	Death in 30 minutes.	195
Mouse	inh	MLC	40-45 mg/l; 7900 ppm	Exposure 2 hrs.	1938
Guinea Pig (young)	inh	LC	200 mg/l; 37,200 ppm	Continuous exposure; death in 9 - 12 min.	1907
Guinea Pig (mature)	inh	LC	200 mg/l; 37,200 ppm	" ; " 40 min.	1907
Rabbit	inh	LC	107.6 mg/l; 20,000 ppm	" ; " 2 hours.	2160
Rabbit	inh	LC	53.8 mg/l; 10,000 ppm	" ; " 2½ hours.	2160
Rabbit	inh	LC	26.9 mg/l; 5000 ppm	" ; " 14-28 hrs.	2160
Rabbit	inh	LC	5.4 mg/l; 1000 ppm	" ; " 28-41 hrs.	2160

2) Repeated dosages; sub-acute, sub-chronic, chronic toxicity; higher animals:
   a) Rabbit: Dermal application 7.7 cc 3 times per day gave death in 4 days; 6.6 and 3.8 cc 3 times per day re- 2160
   sulted in death in 5 days.
   b) Cat: Inhalation exposure to 6.5 - 7.7 mg/l (1200 - 1400 ppm) 8 - 9 hrs per day, 6 days per week for up to 1963
   20 days: Deaths after 2, 3, 7, 11, 18 days with marked loss of weight and reduced body temperature.
   c) Rat: Exposure to 3000 ppm 7 hrs per day for 27 exposures in 36 days yielded mild depression in first week; 11
   beginning 2nd week: Salivation, restlessness, high excitability; prompt recovery after cessation of exposure.
   Rabbits, exposed in like manner, showed no growth retard with minor effects on coordination and equilibrium.
   d) Rat, Guinea Pig, Rabbit, Monkey exposed to 400 ppm 173 times in 243 days showed no deleterious effects. 11
   At 20,000 ppm for 24 minutes showed 100% survival; at 12,000 ppm for 36 minutes showed 100% survival; at 6400 ppm for 84 minutes, showed 100% survival; at 3000 ppm for 420 minutes showed 100% survival. No deleterious effects from exposures at 20,000 ppm for 18 minutes, 12,000 ppm for 36 minutes, 4800 ppm for 84 minutes, 3000 ppm for 300 minutes.
      (1) Maximum Tolerated Concentration, repeated exposure over 6 months:
      Monkeys = 400 ppm; rats, rabbits = 200 ppm; Guinea pigs = 100 ppm.
      (2) 4800 ppm and over give complete anesthesia in rats; 3000 ppm does not yield complete anesthesia in rats.
   e) Rat, Dog: Exposed at 2000 ppm for 6 months: No growth retard, but a slight drowsiness noted; at 3000 ppm 353
   caused more than 50% mortalities; at 4000 ppm gave complete anaesthesia + 100% mortalities.

3) Pharmacological, pharmacodynamic, physiological, etc., higher animals:
   a) Produces a more rapid analgesic effect than any other anesthetic agent. 851
      (1) Prolonged inhalation yields unconsciousness accompanied by marked tachypnea and serious heart irregularities. Not recommended for anesthesia.
      (2) As adjuvant to nitrous oxide + O_2 anesthesia at 0.25 - 0.75% of gas mixture, prolonged amnesia has been caused as well as protracted unconsciousness.
      (3) A primary sign of overdosage is increase in respiratory rate.
   b) Routes of entry to the animal body: Via lungs, with greatest absorption during first few minutes until 1963
   equilibrium is established; via the unbroken skin to a moderate extent; via gastro-intestinal portal. Rapid 2788
   diffusion to all organs occurs with greatest concentration in fat and brain. 2926,956,1493
   c) Fate in body: Metabolized, then partly excreted as trichloroacetic acid, and other unknown metabolites. 3199
   Excretion via lungs as trichloroethylene and via kidneys as trichloroacetic acid and unidentified metabolites. 956
   d) Effects on organ systems: Depressant action on CNS; however, only high concentrations and prolonged ex- 1961
   posure bring complete narcosis. 1963,641
      (1) Narcotic concentration for mice = 25 mg/l (0.0019 M/l) compared to 20 mg/l (0.0017 M/l) for chloro- 1938
      form.
      (2) Depressant action on the heart in situ and in vitro. In the peripheral circulation both vasoconstriction 3199
      and vasodilation effects have been noted.
      (3) Used as an anesthetic, trichloroethylene does not promote good muscle relaxation. 851
      (4) Metabolic effects are not clear-cut in acute poisoning and in chronic poisoning may be referable to liver 3199
      and kidney pathological effects.
   e) Pathology:
      (1) Liver damage has been reported by many (under various experimental circumstances) ranging in degree 3199
      from slight to severe. In general, liver damage is said to be less than with other chlorinated hydrocarbons. There are indications that the damage is reversible in time after cessation of exposure in surviving subjects.
      (2) Kidney damage is reported, including cloudy swelling, congestion, hyperaemia, fatty infiltration, acute 3199
      toxic nephritis with lesions in the convoluted tubules but not in the glomeruli.
      (3) Lung pathologies have been noted by some, and include emphysema, atelectasis, hyperaemia, fatty 3199
      degeneration of the alveolar epithelium, consolidation and desquamation of bronchioles.
   f) Symptoms and signs of exposure: Local signs such as mucous membrane irritation and conjunctivitis; ir- 3199
   ritation and blistering of skin on prolonged contact. Nervous system manifestations: Excitement, signs of drunkeness; headache, dizziness, vertigo, ringing in the ears, difficulties of gait, tiredness, sleepiness, all of which signs may be aggravated by severe exposure. High concentrations may lead to unconsciousness, coma and even convulsions. Mental depression and memory loss may occur. Visual disturbances, and even optic atrophy and blindness, have been reported. Repeated inhalation may lead to craving and habituation, with feelings of well-being and a sense of superior performance following use. Loss of inhibitions, irritability and nervousness may follow such abuse. The exposed subject may suffer chest oppression, pain (substernal and anginal) bradycardia and reduced blood pressure. Even myocardial damage has been claimed. Lung irritations (with cough and over-secretion of mucus and oedema) and various gastro-intestinal signs may attend acute or chronic exposures.
   g) Death from trichloroethylene acute poisoning is in respiratory paralysis and in some cases in cardiac 3199
   failure and/or lung oedema.

3) Toxicity for insects:
   a) Quantitative:

Insect	Route	Dose	Dosage	Remarks	412
Cimex lectularius	Fumig	LC_{50}	67 mg/l	Egg reported to be the most resistant stage.	416
Ephestia kühniella	Fumig	LC_{50}	204 mg/l		416

a) Quantitative (Continued):

Insect	Route	Dose	Dosage	Remarks	
Limonius canus Limonius californicus	Fumig	LC_{50}	168.6 mg/l	Exposure 5 hrs, 77°F, in soil.	1958
Sitophilus granarius (adult)	Fumig	LC_{50}	335 mg/l	Exposure 5 hrs, 25°C, empty vessel fumigation.	156 2816
Sitophilus granarius (adult)	Fumig	LC_{50}	251 mg/l		416
Sitophilus granarius (adult)	Fumig	LC_{99}	405 mg/l	Exposure 5 hrs, 25°C, empty vessel fumigation.	416
Sitophilus oryzae (adult)	Fumig	LC_{50}	219 mg/l		416
Sitophilus oryzae (adult)	Fumig	LC_{50}	196 mg/l	" " "	156,2816
Sitophilus oryzae (adult)	Fumig	LC_{99}	316 mg/l	" " "	156,2816
Tineola biselliella	Fumig	LC_{50}	176 mg/l		416
Tribolium castaneum (adult)	Fumig	LC_{50}	103 mg/l		416
Tribolium confusum (adult)	Fumig	LC_{50}	108 mg/l	" " "	156,2816
Tribolium confusum (adult)	Fumig	LC_{99}	268 mg/l	" " "	2293,2816
Sitophilus granarius (adult)	Fumig	LC_{50}	190 mg/l	" " "	984
Sitophilus oryzae (adult)	Fumig	MLC_{100}	650 mg/l	Exp. 24 hrs at ca.25°C, in 500cc flasks with ca. 250 cc wheat.	2670

187

TRIETHYL TIN HYDROXIDE AND ITS ESTERS; INSECTICIDAL ACTIVITY

Blum, M. S., and Bower, F. A., The Journal of Economic Entomology 50(1): 84, 1957.*

* Attention was drawn to these recently published data too late for inclusion of the source in the cumulative, alphabetic bibliography of this work.

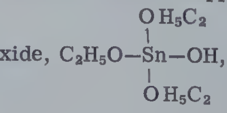
GENERAL

The compounds above, whose toxic properties for Musca domestica have been evaluated, include a number of "organotin" substances, namely the esters formed by triethyl tin hydroxide with 6 organic acids. These esters are the formate, acetate, acrylate, benzoate, bis-(p-chlorophenyl) acetate, and d-trans-chrysanthemumate esters. Each of these esters and the triethyl tin hydroxide itself was found, under the conditions of testing, to induce rapid paralysis and death at very low dosage levels in Musca domestica adults of two biotypes viz., DDT-non R (Chemical Specialties Manufacturers Association biotype) and DDT-R (the Orlando-Beltsville biotype). The esters were found not to inhibit choline esterase(s) at concentrations to 1 times 10^{-3} M. The esters blocked conduction in the isolated nerve cord of Periplaneta americana completely. The esters, in vitro, inhibited phosphorylations associated with rat brain and liver mitochondria systems. A slightly greater toxicity of the esters for DDT-non R Musca, as compared with DDT-R Musca, has been noted.

TOXICOLOGICAL

1) Vs. higher animals:
   a) In contrast with inorganic tin salts, triethyl tin acetate has been reported as highly toxic for frog, dog and rabbit.
      (1) Indications are that tin is essentially non-toxic in the ionic state but highly toxic in the non-ionic state, an attribute exceptional among the heavy metal compounds.

2) Toxicity for insects:
   a) Patents have been granted for tetra-alkyl- and tetra-aryl-tin compounds as moth-proofing agents, as well as for organic compounds of quadrivalent tin having one tin atom per molecule, for all of which moth-proofing qualities are asserted. (I. G. Farben industrie Aktion-Gesellschaft Dutch Patent 20,570 and British Patent 303,092, Hartmann, E., et al., U. S. Patent 1,744,633, German Patent 485,646 and Namloze Venootschap de Bataafsche Petroleum Maatschappij Dutch Patent 68,578.)

   b) Toxicity of triethyl tin hydroxide,  $C_2H_5O-\underset{\overset{|}{OH_5C_2}}{\overset{\overset{OH_5C_2}{|}}{Sn}}-OH$, and various of its esters:

(1) Musca domestica imagines, ♂ and ♀, 3 - 4 days old, treated topically by the measured drop method with the esters in acetone solution; 20 insects per test group held at 30°C post-treatment:

Compound	Dose (μg/fly)	% Mortality (24 Hrs.)		LD$_{50}$ 24 Hrs. (μg/fly)	
		DDT-non R	DDT-R	DDT - non R	DDT-R
Triethyl tin hydroxide	0.10	20	10	0.31	0.40
	.25	45	30		
	.50	70	55		
	.75	100	80		
Triethyl tin formate	0.10	35	5	0.25	0.45
	.25	50	25		
	.50	70	55		
	.75	95	90		
Triethyl tin acetate	0.10	15	15	0.30	0.54
	.25	40	25		
	.50	90	45		
	.75	100	75		
Triethyl tin acrylate	0.10	10	--	0.42	0.70
	.25	30	20		
	.50	70	35		
	.75	95	60		
	1.0	--	95		
Triethyl tin benzoate	0.25	10	--	0.52	0.74
	.50	35	20		
	.75	70	55		
	1.0	90	75		
	1.5	--	100		
Triethyl tin d-trans-chrysanthemumate	0.25	15	--	0.51	0.98
	.50	45	15		
	.75	75	35		
	1.0	100	55		
	1.5	--	90		
Triethyl tin bis (p-chlorophenyl) acetate	0.50	20	--	0.76	1.28
	.75	35	15		
	1.0	65	35		
	1.5	95	60		
	2.0	--	85		

188

WILFORDINE (Wilforine)

$C_{43}H_{49}O_{19}N$

GENERAL [Refs.: 226, 225]

The alkaloids of the plant Tripterygium wilfordii have long been used by the Chinese as an insecticide in the form of the powdered roots. These alkaloids are now recognized as having an insecticidal action on certain chewing insects, for example the young larvae of Pyrausta nubilalis, Plutella maculipennis, Carpocapsa pomonella, and others. The substance called Wilfordine, which as a crystalline substance shows a high toxicity toward the larvae of Carpocapsa pomonella, is in reality a mixture of 5 similar alkaloids all of which are insecticidally active.

PHYSICAL, CHEMICAL

A mixture of 5 similar alkaloids: Wilfordine, wilforine, wilforgine, wilfortrine, wilforzine; molecular weight ca. 900; complex esters, the first four of the five mentioned above possess a polyhydroxy-nucleus with 8 of the 10 hydroxyl groups esterified in the case of the intact alkaloid, 5 with acetic acid, 1 with benzoic acid or 3-furoic acid, 2 with a nitrogen-containing dicarboxylic acid. The dicarboxylic acid is a 2-substituted nicotinic acid derivative. Wilforzine has the same constitution save that it has one less acetyl group.

TOXICOLOGICAL

1) Toxicity for higher animals:
   a) Fed in baits to rats as 20% ground whole root of Tripterygium wilfordii, as 0.5% non-crystalline alkaloid(s) or as 0.5% crystalline alkaloid(s) no symptoms of poisoning resulted.

2) Toxicity for insects:
   a) Toxicity to newly hatched larvae of Pyrausta nubilalis fed on corn leaves treated with a spray containing 60 ppm of pure alkaloid:

Alkaloid	% Mortality After	
	2 Days	3 Days
Wilforine	88	100
Wilforgine	30	54
Wilfordine	54	100
Wilfortrine	48	73

   (1) Corn leaves sprayed with a solution containing 60 ppm of a non-crystalline fraction of extracted Tripterygium yielded a 90% mortality of Pyrausta nubilalis in 2 days.
   (2) Sprays, made up of 4 lbs of root powder per 100 gallons water yielded 81% and 96% mortalities of Pyrausta after 48 and 72 hours, respectively.
   (3) In the case of Plutella maculipennis larvae, wilforzine is toxic but less so than wilforine.

   b) Tripterygium wilfordii root powders are effective vs. the following insects, with the smaller larvae being, in general, more potently affected than the larger: Gastrophyse cyanea (3rd instar), Anthonomus eugenii. Some toxicity is manifested vs. larvae of Epilachna varivestis (3rd, 4th instars), Evergestis rimosalis (4th instar), Pseudaletia unipuncta (1st, 3rd instars), Phlyctaenia rubigalis (3rd instar), Hymenia recurvalis (2nd instar).
   (1) Root powders are ineffective vs.: Heliothis armigera (5th instar), Oncopeltus fasciatus, Estigmene acraea (3rd instar), Macrosiphum pisi, Bruchus pisorum, Autographa öo (4th instar), Callitroga hominivorax, Epicauta spp. (adults), Epilachna varivestis (adults).
   (2) Limonius canus, Limonius californicus were not affected by hot water, 1% acetone or ethanol extractives of Tripterygium.
   (3) Tetranychus bimaculatus (nymphs, adults) was not affected by the root powders.
   (4) Diaphania hyalinata and Pieris rapae (3rd, 4th instars) were unaffected by root powders.
   (5) 50 mg/cc in deobase oil proved non-toxic for Musca domestica. No synergism was manifested with pyrethrins.
   (6) Vs. Musca domestica, the non-crystalline alkaloid fraction proved ineffective as an ingredient of baits.
   (7) Vs. mosquito larvae, the non-crystalline alkaloid fraction yielded 100% mortality in 48 hours at 10 ppm and 16% mortality at 0.1 ppm.
   (8) Powdered Tripterygium root proved valueless either as a stomach poison or repellent for Popillia japonica.

BIBLIOGRAPHY

1. Abbot, W. S., and Billings, S. C., The Journal of Economic Entomology 28: 493, 1935.
2. Abrams, H. K., and Leonard, A. R., California Medicine (San Francisco) 73: 183, 1950.
3. Abreu, B. E., et al., Anesthésie et analgésie 18: 156, 1939.
4. Abreu, B. E., et al., Proceedings for the Virginia Academy of Science (Lexington, Va., U.S.A.) 40: 48, 1938.
5. Abreu, B. E., and Emerson, G. A., University of California Publications in Pharmacology (Berkeley) 1: 313, 1940.
6. Acree, F., et al., The Journal of Economic Entomology 29: 601, 1936.
7. Ibid., 49(6): 808, 1956.
8. Acree, F., et al., The Journal of Organic Chemistry (Baltimore) 10: 236; 449, 1945.
9. Acree, F., et al., The Journal of Organic Chemistry (Baltimore) 12: 731, 1947.
10. Adams, E. M., et al., Archives of Industrial Hygiene and Occupational Medicine 1: 225, 1950.
11. Adams, E. M., et al., Archives of Industrial Hygiene and Occupational Medicine 4: 469, 1951.
12. Adams, E. M., et al., The Journal of Industrial Hygiene and Toxicology 22: 79, 1940.
13. Adams and Whittaker, Biochimica et biophysica acta (Amsterdam) 3: 1, 1949.
14. Adrian, E. D., et al., British Journal of Pharmacology and Chemotherapy 2: 56, 1947.
15. Aeschlimann, J. A., and Reinert, M., The Journal of Pharmacology and Experimental Therapeutics 43: 413, 1931.
16. Ahmed, M. K., et al., The Journal of Economic Entomology 47(3): 445, 1954.
17. Ibid., 47(4): 684, 1954.
18. Ahmed, M. K., The Journal of Economic Entomology 48(5): 530, 1955.
19. Akamatsu, M., and Watanabe, K., Botyu Kagaku (Kyoto) 16: 90, 1951.
20. Albaum, H. G., et al., The Journal of Biological Chemistry 163: 641, 1946.
21. Albert, W. B., South Carolina Agricultural Experiment Station Annual Report No. 44, 1931, p. 47.
22. Ibid., No. 45, 1932, p. 44.
23. Albert, W. B. and Paden, W. R., Science 73: 622, 1931.
24. Aldridge, W. N., Biochemical Journal (London) 46: 451, 1950.
25. Ibid., 53: 62, 1953.
26. Ibid., 53: 110, 1953.
27. Ibid., 53: 117, 1953.
28. Ibid., 54: 442, 1953.
29. Aldridge, W. N., Chemistry and Industry, 1954, p. 473.
30. Aldridge, W. N., and Barnes, J. M., Nature (London) 169: 343, 1952.
31. Aldridge, W. N., and Davison, A. N., Biochemical Journal (London) 51: 62, 1952.
32. Ibid., 52: 663, 1952.
33. Alexander, C. P., Massachusetts Agricultural Experiment Station Bulletin No. 417, 1945.
34. Ibid., No. 428, 1946.
35. Alfaro, A., Boletin de patologia végetal y entomología agrícola (Madrid) 14: 335, 1946.
36. Allen, N., South Carolina Agricultural Experiment Station, 57th Annual Report, p. 114.
37. Ibid., 58th Annual Report, p. 108.
38. Allen, T. C., The Journal of Economic Entomology 38(3): 389, 1945.
39. Allen, T. C., et al., The Journal of Economic Entomology 37: 400, 1944.
40. Ibid., 38(3): 293, 1945.
41. Alles, and Hawes, The Journal of Biological Chemistry 166: 698, 1940.
42. Allmann, S. L., and Freund, A. H., Agricultural Gazette of New South Wales (Australia, Dominion of) 59: 531, 1948.
43. Allmann, S. L., and Wright, J., Agricultural Gazette of New South Wales (Australia, Dominion of) 59: 233, 1948.
44. Almeida, P. R., Archivos do Instituto biológio (de defesa agricola e animal) São Paulo 18: 31, 1947.
45. Alsterlund, J. F., and Compton, C. C., The Journal of Economic Entomology 30: 571, 1937.
46. Althaus, R. E., Data contributed by, on behalf of B. F. Goodrich Chemical Co., Cleveland, Ohio.
47. Aman, J. et al., Annals of Applied Biology 33(4): 389, 1928.
48. Ambrose, A. M., Federation Proceedings (Federation of American Societies for Experimental Biology, Baltimore) 12: 298, 1953.
49. Ambrose, A. M., The Journal of Pharmacology and Experimental Therapeutics 69: 274, 1940.
50. Ambrose, A. M., et al., Archives of Industrial Hygiene and Occupational Medicine 7: 197, 1953.
51. Ambrose, A. M., et al., Journal of the American Pharmaceutical Association 42: 364, 1953.
52. Ambrose, A. M., and Haag, H. B., Industrial and Engineering Chemistry 28: 815, 1936.
53. Ibid., 30: 592, 1938.
54. Ambrose, A. M., and Robbins, D., Federation Proceedings (Federation of American Societies for Experimental Biology, Baltimore) 10: 276, 1951.
55. American Conference of Governmental Industrial Hygienists April, 1952.
56. American Conference of Governmental Industrial Hygienists, Los Angeles, 1953; Archives of Industrial Hygiene and Occupational Medicine 8: 296, 1953.
57. American Cyanamid Co., Technical Bulletin No. 2, 1948.
58. American Cyanamid Co., Data given to United States Food and Drug Administration, 1950.
59. American Medical Association, Committee on Pesticides, Journal of the American Medical Association 144: 104, 1950.
60. American Petroleum Institute, "Manual of Refinery Wastes", Section I, 4th Edition, 1949.
61. American Potash and Chemical Corp., Brochure: "Methyl Bromide, the Versatile Fumigant".
62. American Water Works Association, "Water Quality and Treatment", 1950.
63. Ammann, E., Schweizerische Fischereizeitung (Schweizerischer Fischereiverein, Zurich) 59(5): 143, 1951.

64. Ampola, G., and Tommasi, G., Annali della Reale Stazione chimico-agraria sperimentale di Roma (Italia) 5: 241, 1912.
65. Andersen, A. H., and Jersilt, T., Acta pharmacologica et toxicologica (København) 5: 129, 1949.
66. Anderson A., et al., Annals of the Entomological Society of America 47: 595, 1954.
67. Anderson, B. G., Science 102: 539, 1945.
68. Anderson, B. G., Sewage Works Journal 18: 82, 1946.
69. Anderson, L. D., and Hofmaster, R. N., The Journal of Economic Entomology 41: 334, 1948.
70. Anderson, L. D., and Hook, R. A., The Journal of Economic Entomology 34(5): 725, 1941.
71. Andison, H., Department of Agriculture, Canada (Dominion of), Division of Entomology Publication No. 78, 1948.
72. Andres, L. A., et al., The Journal of Economic Entomology 48(5): 509, 1955.
73. Andrews, H. L., et al., Public Health Reports (Washington, D.C.) 61: 450, 1946.
74. Annand, P. N., Annual Reports, U. S. Bureau of Entomology (U.S. Department of Agriculture) 1945, 1946.
75. Annau, E., et al., Canadian Journal of Medical Sciences 30: 463, 1952.
76. Anonymous, Agricultural Chemicals 1(3): 32, 1946.
77. Ibid., 2(6): 39, 1947.
78. Ibid., 4(4): 30, 1949.
79. Ibid., 4(4): 31, 1949.
80. Ibid., 4(4): 43, 1949.
81. Anonymous, Agricultural Chemicals (Technical Section) 9(6): 93, 1954.
82. Anonymous, in Agricultural Chemicals 10(6): 49, 1955 quoting California Agriculture 9(3): 1955.
83. Anonymous, Agricultural Gazette of New South Wales (Australia, Dominion of) 59: 537, 1948.
84. Anonymous, American Fruit Grower 69(2): 25, 1949.
85. Anonymous, Analytical Chemistry 22: 1219, 1950.
86. Anonymous, Chemistry and Engineering News, 1948, January.
87. Anonymous, Chemistry and Industry 1951, p. 123.
88. Anonymous, Citrus Experiment Station, (Riverside, California) September 12, 1949.
89. Anonymous, "Clinical Memoranda on Economic Poisons", Technical Development Laboratories, Technology Branch, Communicable Disease Center, U. S. Public Health Service, Savannah, Georgia. As Revised April 1, 1955.
90. Ibid., As Revised, 1956.
91. Anonymous, Conference Report on Cotton Insect Research and Control, Baton Rouge, Louisiana November 1948 (Bureau of Entomology, Agricultural Research Administration, U.S. Department of Agriculture, Washington, D.C.).
92. Anonymous, Water Works Engineering 86: 118, 1933, "Control of Vegetation."
93. Anonymous, Engineering News-Record 125: 113, 1940.
94. Anonymous, Industrial Hygiene Newsletter No. 19, 1949.
95. Anonymous, Journal of the American Medical Association 149: 1135, 1952.
96. Anonymous, New Jersey Department of Agriculture Annual Report 1926, p. 71.
97. Anonymous, Ohio Agricultural Experiment Station Bulletin No. 599, 1939.
98. Anonymous, Annual Reports of the Bureau of Sugar Experiment Stations, Queensland (Australia, Dominion of) 1938, 1948.
99. Anonymous, Report of the California Agricultural Experiment Station for 1930 - 1931, p. 67.
100. Anonymous, Report No. 7, Environmental Health Center, U. S. Public Health Service, 1951, p. 13.
101. Anonymous, "Research Newsletter" quoting the National Institutes of Health in Journal of Agricultural and Food Chemistry 3(4): 277, 1955.
102. Anthon, E. W., The Journal of Economic Entomology 44(6): 1012, 1951.
103. Ibid., 48(1): 56, 1955.
104. Antoniani, C., and Fonio, G., Atti della Reale Accademia (Nazionale) dei Lincei Rend. Cl. Sci. Fis. Mat. e Nat. 9: 344, 1929, (Roma).
105. Apple, J. W., and Decker, G. C., The Journal of Economic Entomology 42(1): 88, 1949.
106. Ibid., 43(4): 407, 1950.
107. Apple, J. W., and Martin, R., The Journal of Economic Entomology 48(2): 193, 1955.
108. Apple, J. W., and Richardson, C. H., The Journal of Economic Entomology 37(5): 666, 1944.
109. Arant, F. S., The Journal of Economic Entomology 35(6): 873, 1942.
110. Ibid., 41: 26; 803. 1948.
111. Ibid., 45(1): 121, 1952, quoting data of Richards, H., Thesis.
112. Armand, J. E., Annual Report of the Entomological Society of Ontario (Canada) 1947, p. 15.
113. Armitage, California Department of Agriculture Bulletin 35: 21, 1946.
114. Armstrong, G., et al., Annals of Applied Biology 38: 555, 1951.
115. Ibid., 39: 548, 1952.
116. Armstrong, T., Department of Agriculture, Canada (Dominion of), Division of Entomology Publication No. 34, 1945.
117. Armstrong, T., The Canadian Entomologist 82(4): 73, 1950.
118. Armstrong, T., Down to Earth 6(1): 1950.
119. Armstrong, T., "Report on Acaricide Investigations". Dominion Entomological Laboratory, Vineland Station, Ontario, Canada Parts I, II, 1947.
120. Armstrong, T., Scientific Agriculture (Canada, Dominion of) 29: 81, 1949.
121. Arnason, A. P., et al., The Canadian Entomologist 79: 174, 1947.
122. Asano, M., and Kanematsu, T., Berichte; Deutsche chemische Gesellschaft. (Berlin) 65B: 1602, 1932.
123. Ashby, D. G., Annals of Applied Biology 37: 624, 1950.
124. Ashdown, D., et al., The Journal of Economic Entomology 45(1): 82, 1952.
125. Ashdown, D., and Cordner, H. B., The Journal of Economic Entomology 45(2): 302, 1952.
126. Asquith, D., The Journal of Economic Entomology 47(3): 457, 1954.
127. Asquith, D., and Kana, N. F., The Journal of Economic Entomology 45(1): 60, 1952.
128. Association of British Insecticide Manufacturers, "British Insecticides and Fungicides", London, 1948.
129. Association of Economic Poisons Control Officials Inc., Official Publication of, 1954.
130. Atkeson, F. W., et al., The Journal of Economic Entomology 37: 428, 1944.

131. Atkins, E. L., and Anderson, L. D., The Journal of Economic Entomology 47(6): 969, 1954.
132. Attia, R., Royal Ministry of Agriculture (Egypt), Tech. Sci. Service Bulletin No. 105, 1931.
133. Augustinsson, K. B., Acta physiologica Scandinavica (Stockholm) 15: supplement 52, 1948.
134. Augustinsson, K. B., Arkiv Kemi 6(31): 331, 1953.
135. Augustinsson, K. B., Svensk Kemisk Tidskrift 64: 87, 1952.
136. Augustinsson, K. B., "The Enzymes" Vol. I, Academic Press, New York, 1950.
137. Augustinsson, K. B., and Grahn, M., Acta chimica Scandinavica 7: 906, 1953.
138. Augustinsson, K. B., and Grahn, M., Acta physiologica Scandinavica (Stockholm) 32: 174, 1954.
139. Augustinsson, K. B., and Nachmansohn, D., Science 110: 98, 1949.
140. Ault, C. N., Nature (London) 157: 699, 1946.
141. Austin, L., and Berry, W., Biochemical Journal (London) 54: 695, 1953.
142. Austin, L., and Davies, D. R., Proceedings of the Royal Society of Medicine. London. 46: 802, 1953.
143. Averell, P., and Norris, M., Analytical Chemistry 20: 753, 1948.
144. Avery, S., Journal of the American Chemical Society 28: 1155, 1906.
145. Avery, S., and Beans, H. T., Journal of the American Chemical Society 23: 111, 1901.
146. Baader, E. W., Archiv für Hygiene und Bakteriologie 132: 219, 1950.
147. Babers, F. H., Journal of Agricultural Research (Washington D.C.) 63: 183, 1941.
148. Babers, F. H., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine No. E-776, 1949.
149. Babers, F. H., and Culpeper, G., The Journal of Parasitology 35: 551, 1949.
150. Babers, F. H. and Mitlin, N., The Journal of Economic Entomology 48(4): 430, 1955.
151. Babers, F. H., and Pratt, J. J., in "Insects". The Yearbook of Agriculture, 1952. U.S. Department of Agriculture, Washington, D.C.
152. Babers, F. H., and Pratt, J. J., The Journal of Economic Entomology 46: 977, 1953.
153. Babers, F. H., and Pratt, J. J., Physiological Zoölogy 23: 58, 1950.
154. Babers, F. H., and Pratt, J. J., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine No. 818, 1951.
155. Back, E. A., U.S. Department of Agriculture Farmer's Bulletin No. 1670, 1932.
156. Back, E. A., and Cotton, R. T., U.S. Department of Agriculture Circular No. 369, 1935.
157. Back, R., Contributions from the Boyce Thompson Institute 16: 451, 1951.
158. Bacon, O. G., The Journal of Economic Entomology 43: 364, 1950.
159. Bado, A. A., Journal of the American Water Works Association 31: 1975, 1939.
160. Baker, (J. T.) Chemical Company, "DDT" 1945.
161. Bain, J. A., Proceedings of the Society for Experimental Biology and Medicine 72: 9, 1949.
162. Bakke, A. L., Agronomy Journal 33: 759, 1941.
163. Balaban, I. E., and Sutcliffe, F. K., Nature (London) 155: 755, 1945.
164. Baldwin, E., "Dynamic Aspects of Biochemistry", Cambridge University Press, 1947.
165. Ball, H. J., and Allen T. C., The Journal of Economic Entomology 42: 394, 1949.
166. Ball, H. J., and Beck, S. D., The Journal of Economic Entomology 44(4): 558, 1951.
167. Ball, R. C., Transactions. The American Fisheries Society 75: 36, 1945.
168. Ibid., 75: 139, 1945.
169. Ball, W. G., Archives of Industrial Hygiene and Occupational Medicine 7: 292, 1953.
170. Balls, A. K., and Jansen, E., Advances in Enzymology and Related Subjects of Biochemistry 13: 321, 1952.
171. Balson, E., Transactions; The Faraday Society 43: 54, 1947.
172. Bandt, H. J., Beitraege zu Wasser, Abwasser und Fischereichemie 1: 42, 1946.
173. Bandt, H. J., Gesundheits - Ingenieur 63: 19, 1940.
174. Bandt, H. J., Mitteilungen der Fischerei-verein, Ost Ausgabe 25(10): 165, 1933. Water Pollution Abstracts 7: March, 1934.
175. Bann, J. B., et al., Pre- Publication Data of Shell Development Co., Agricultural Research Division. Contributed by Hamman, R. E., 1956.
176. Bannister, et al., The Journal of Physiology (London) 115: 55, 1951.
177. Barber, G. W., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine E-485, 1939.
178. Barber, G. W., U.S. Department of Agriculture, Technical Bulletin No. 880, 1944.
179. Barber, G. W., and Schmitt, J. B., The Journal of Economic Entomology 42: 844, 1949.
180. Barber, G. W., and Schmitt, J. B., New Jersey Agricultural Experiment Station Bulletin No. 742, 1948.
181. Bare, C. O., The Journal of Economic Entomology 41(1): 13, 1948.
182. Bargioni, G., et al., Rivista della Ortoflorofrutticoltura italiana (Firenze) 36: 263, 1952.
183. Barke, A., Tierärztliche Umschau (Konstanz) 5: 61, 1950.
184. Barnes, J. M., Proceedings of the Second International Congress of Plant Protection, London 1949, Volume II p. 14.
185. Barnes, J. M., "Toxic Hazards of Certain Pesticides to Man", World Health Organization Monograph Series No. 16, Palais des Nations, Genève, 1953.
186. Barnes, J. M., World Health Organization Bulletin 8: 419, 1953.
187. Barnes, J. M., and Davies, D. R., The British Medical Journal 2: 816, 1952.
188. Barnes, J. M., and Denz, F. A., The British Medical Journal 1: 11, 1954.
189. Barnes, J. M., and Denz, F. A., The Journal of Hygiene (London) 49: 430, 1951.
190. Barnes, J. M., and Denz, F. A., The Journal of Pathology and Bacteriology (London) 65: 597, 1953.
191. Barnes, M. M., The Journal of Economic Entomology 44(5): 672, 1951.
192. Barnes, M. M., et al., The Journal of Economic Entomology 47(2): 238, 1954.
193. Barrett, H., et al., Journal of Industrial Hygiene and Toxicology 21: 479, 1939.
194. Barry, G., and Boyer, R., Canadian Journal of Research B26: 511, 1948.
195. Barsoum, G. S., and Saad, K., Quarterly Journal of Pharmacy and Pharmacology (London) 7: 205, 1934.

196. Barthel, W. F., et al., Journal of the American Chemical Society 76: 4186, 1954.
197. Barthilhemy, N. L., Journal of Industrial Hygiene and Toxicology 21: 141, 1939.
198. Bartlett, B., and Ewart, W. H., The Journal of Economic Entomology 44(3): 344, 1951.
199. Basinger, A. J., and Boyce, A. M., The Journal of Economic Entomology 29: 161, 1936.
200. Bateman, G. Q., et al., Journal of Agricultural and Food Chemistry 1: 322, 1953.
201. Batt, R. F., et al., Annals of Applied Biology 41: 475, 1954.
202. Batte, E. G., Veterinary Medicine 48(8): 319, 1953.
203. Batte, E. G., and Turk, R. D., The Journal of Economic Entomology 41(1): 102, 1948.
204. Bauer, Federation Proceedings 9: 257, 1950.
205. Bayer, German Patent No. 817, 753 (1951).
206. Beard, R. L., The Journal of Economic Entomology 42(2): 292, 1949.
207. Beauregard, J. R., et al., Journal of Agricultural and Food Chemistry 3(2): 124, 1955.
208. Bechold, Zeitschrift für physiologische Chemie (Hoppe-Seylers') 47: 173, 1906.
209. Beck, Proceedings of the Society for Experimental Biology and Medicine 78: 392, 1951.
210. Behrend, The Journal of Pharmacology and Experimental Therapeutics 48: 317, 1933.
211. Belding, D. L., Transactions. The American Fisheries Society 57: 100, 1927.
212. Bellamare, E., and Belcourt, J., The Canadian Entomologist 85: 449, 1953.
213. Belleuvre, G., Annales de physiologie et de physicochimie biologique (Paris) 14: 717, 1938.
214. Bender, H., and Pitt, H., U.S. Patent No. 2, 593, 001 (1952).
215. Bennett, G., Outline, Illinois Custom Spray Operators' School, Urbana, Illinois 1949, p. 27.
216. Bennett, S. H., Annals of Applied Biology 36: 160, 1949.
217. Bennett, S. H., et al., Annals of Applied Biology 33: 396, 1946.
218. Bennett, S. H., et al., Annual Report, Long Ashton Research Station, Bristol (University of), (Great Britain) 1948, p. 138.
219. Bennett, S. H., and Thomas, W.D.E., Annals of Applied Biology 41: 484, 1954.
220. Bennett, S. H., and Thomas, W.D.E., Transactions of the 9th International Congress of Entomology, Amsterdam 1951, Volume I, p. 982.
221. Bennison, B. E., and Mostofi, F. K., Journal of the National Cancer Institute (Washington, D.C.) 10: 989, 1950.
222. Beran, F., Proceedings of the First International Congress of Plant Protection, Heverlee (The Netherlands) 1946, p. 429.
223. Bernheim, F., "Interaction of Drugs and Cell Catalysts". Burgess, Minneapolis, 1948.
224. Beroza, M., Analytical Chemistry 26: 1173, 1954.
225. Beroza, M., Journal of The American Chemical Society 73: 3656, 1951.
226. Beroza, M., and Bottger, G. T., The Journal of Economic Entomology 47(1): 188, 1954.
227. Berry, C. E., California Department of Agriculture Bulletin 27: 172, 1938.
228. Berry, E. G., et al., Public Health Reports 65: 1950.
229. Berry, R. C., The Journal of Economic Entomology 43(1): 112, 1950.
230. Bertholf, J. H., Proceedings; Florida Anti-Mosquito Association 1950, p. 80.
231. Bertholf, L. M., and Pilson, J. E., The Journal of Economic Entomology 34(1): 24, 1941.
232. Bertram, S., et al., Biochemische Zeitschrift 197: 1, 1928.
233. Bibby, F. F., The Journal of Economic Entomology 35: 193, 1942.
234. Biddulph, C., et al., Advances in Chemistry Series 1: 237, 1950.
235. Biddulph, C., et al., Journal of Dairy Science 35: 445, 1952.
236. Bidstrup, P. L., The British Medical Journal 2: 548, 1950.
237. Bidstrup, P. L., Proceedings of the Royal Society of Medicine 45: 574, 1952.
238. Bidstrup, P. L., Proceedings of the Second International Congress of Plant Protection, London, 1949, p. 23.
239. Bidstrup, P. L., et al., The British Medical Journal 2: 273, 1950.
240. Bidstrup, P. L., et al., Lancet 1952, p. 794.
241. Bidstrup, P. L., and Hunter, Lancet 1952, p. 262.
242. Billet, and Abel, Gazette des hopitaux (civils et militaires) (Paris) 113: 464, 1940.
243. Billings, S. C., The Journal of Economic Entomology 35(2): 289, 1942.
244. Bing, R. J., et al., Bulletin of the Johns Hopkins Hospital (Baltimore) 78: 308, 1946.
245. Bishop, E. L., Science 92: 201, 1940.
246. Bishopp, F. C., American Journal of Public Health 36: 593, 1946.
247. Bishopp, F. C., Journal of the American Water Works Association 40: 264, 1948.
248. Bishopp, F. C., The Journal of Economic Entomology 39: 449, 1946.
249. Blacklith, R. E., Annals of Applied Biology 40: 106, 1953.
250. Blacklith, R. E., Journal of the Science of Food and Agriculture 3: 219, 1952.
251. Ibid., 3: 224, 1952.
252. Ibid., 3: 482, 1952.
253. Blacklith, R. E., Pyrethrum Post 3(2): 20, 1953.
254. Blalock, J. W., Science 114: 122, 1951.
255. Blalock, J. W., and Lindgren, D. L., The Journal of Economic Entomology 44(5): 657, 1951.
256. Blanchard, R. A., and Chamberlin, J. R., The Journal of Economic Entomology 41: 928, 1948.
257. Blauvelt, W. E., New York State Flower Growers' Bulletin 2: 6, 1945.
258. Blauvelt, W. E., Florists' Exchange 108: 15, 1947 quoted by Brown, A.W.A., "Insect Control by Chemicals", 1950.
259. Blickle, R. L., et al., Soap and Sanitary Chemicals 24(8): 58, 1948.
260. Blinn, R., et al., Journal of the American Chemical Society 76: 37, 1954.
261. Blinn, R., and Gunther, F., Journal of the American Chemical Society 72: 1399, 1950.
262. Bliss, C. I., Annals of the Entomological Society of America 33: 721, 1940.
263. Bliss, C. I., Annals of Applied Biology 26: 586, 1939.
264. Blitz, W., Berichte; Deutsche chemische Gesellschaft. 37: 3138, 1904.
265. Bloch, Helvetica medica Acta (Basel) 7: (supplement 8) 15, 1941.
266. Block, S. S., Soap and Sanitary Chemicals 24(2): 138, 1948.
267. Ibid., 24(3): 151, 1948.

268. Ibid., 24(4): 155, 1948.
269. Bluestone, H. R., U.S. Patent 2, 676, 132 (1954).
270. Bluestone, H. R., et al., U.S. Patent 2, 576, 666 (1951).
271. Blum, M. S., and Kearns, C. W., The Journal of Economic Entomology 49(2): 283, 1956.
272. Ibid., 49(4): 496, 1956.
273. Ibid., 49(6): 862, 1956.
274. Bobb, M. L., The Journal of Economic Entomology 42: 343, 1949.
275. Ibid., 43(1): 157, 1950.
276. Bodansky, O., Annals of the New York Academy of Sciences 47: 521, 1946.
277. Bodenstein, D., The Biological Bulletin 90: 148, 1946.
278. Bodine, J. H., and Boell, E. J., Journal of Cellular and Comparative Physiology 11: 41, 1938.
279. Bodine, J. H., and Boell, E. J., Proceedings of the Society for Experimental Biology and Medicine. 35: 504, 1936.
280. Bohart, R. M., The Journal of Economic Entomology 35(3): 365, 1942.
281. Ibid., 36: 442, 1943.
282. Bohart, R. M., and Murray, W. D., Proceedings of the 18th Annual Conference of the California Mosquito Control Association 1950, p. 20.
283. Bolle, W., Veterinärmedizinische Nachrichten, 1953, part 3/4.
284. Bond, J. A. B., Bulletin of Entomological Research (London) 44: 97, 1953.
285. Bondy, F. F., and Rainwater, C. F., 57th Annual Report of the South Carolina Experiment Station, 1943-1944.
286. Ibid., 58th Annual Report, 1946.
287. Bonnemaison, L., Proceedings of the First International Congress of Plant Protection, Heverlee (The Netherlands) 1947, p. 227.
288. Bonsmann, Klinische Wochenschrift (Berlin) 21: 304, 1942.
289. Booer, J. R., Annals of Applied Biology 31: 340, 1944.
290. Borchert, A., Archiv für Bienenkunde (Leipzig) 10: 1, 1929.
291. Borden A., and Madsen, H., Western Fruit Growers 8(1): 23; 8(2): 29, 1954.
292. Borglin, J., U.S. Patent 2, 717, 611 (1941).
293. Bosse, G. H. L., Höfchen-Briefe für Wissenschaft und Praxis (Bayer Pflanzenschutz Nachrichten) 5: 81, 239, 1952.
294. Boswell, V. R., in "Insects", The Yearbook of Agriculture, 1952. U.S. Department of Agriculture, Washington, D.C.
295. Bot, J., Documenta de Medicina Geographica et Tropica 4: 57, 1952.
296. Böttcher, F. K., Zeitschrift fur angewandte Entomologie (Berlin) 25:419, 1939.
297. Ibid., 25: 681, 1939.
298. Bottger, G. T., and Bowen, C. V., U.S. Department of Agriculture Bureau of Entomology and Plant Quarantine E-710, 1946.
299. Bottger, G. T., and Gertler, S. I., The Journal of Economic Entomology 42(4): 611, 1949.
300. Bottger, G. T., and Levin, C., The Journal of Economic Entomology 39(4): 539, 1946.
301. Bottger, G. T., and Yerington, A. P., The Journal of Economic Entomology 44(2): 261, 1951.
302. Ibid., 45(1): 131, 1952.
303. Bouchet, R. L., Compte Rendu, III$^{\text{eme}}$ Congrès international de phytopharmacie, Paris 1952, p. 221.
304. Bourcart, E., "Insecticides, Fungicides, Weed-Killers". E. Benn, London, 1926.
305. Bourne A. I., and Shaw, F. R., The Journal of Economic Entomology 40: 429, 1947.
306. Boursnell, J. C., and Webb, E. C., Nature (London) 164: 875, 1949.
307. Boush, G. M., The Journal of Economic Entomology 47(1): 98, 1954.
308. Bousquet, E., U.S. Patent No. 2, 402, 530 (1945).
309. Ibid., No. 2, 405, 559 (1946).
310. Ibid., No. 2, 424, 220 (1947).
311. Bousquet, E., et al., Industrial and Engineering Chemistry 27: 1342, 1935.
312. Bovingdon, H. H. S., and Coyne, F. P., Annals of Applied Biology 31: 255, 1944.
313. Bowen, C. V., and Barthel, W., The Journal of Economic Entomology 36: 627, 1943.
314. Bowen, C. V., and Hall, S. A., in "Insects", The Yearbook of Agriculture, 1952. U.S. Department of Agriculture, Washington, D.C.
315. Boyce, A. M., et al., The Journal of Economic Entomology 32: 432, 1939.
316. Ibid., 32: 450, 1939.
317. Boyce, H. R., 73rd Annual Report of the Entomological Society of Ontario (Canada), 1942.
318. Braceland, F. J., Annals of Internal Medicine 16: 246, 1942.
319. Bradbury, F., et al., Nature (London) 172: 1052, 1953.
320. Bradbury, F., and Standen, H., Journal of the Science of Food and Agriculture 6: 90, 1955.
321. Bradley, R. S., and Cleasby, T. G., Journal of the Chemical Society, 1953, p. 1690.
322. Brann, J. L., Proceedings of the New York Horticultural Society 91: 193, 1946.
323. Brannon, L. W., The Journal of Economic Entomology 38: 101, 1945; 40: 103, 1947.
324. Ibid., 40: 933, 1947.
325. Brannon, L. W., Virginia Agricultural Experiment Station Bulletin No. 85, 1934.
326. Brauer, R. W., The Journal of Pharmacology and Experimental Therapeutics 92: 162, 1948.
327. Brauer, R. W., et al., Federation Proceedings, 6: 311, 1947.
328. Brauer, R. W., and Pessoti, R., Science, 110: 195, 1949.
329. Bredenkamp, J., Zeitschrift für angewandte Entomologie (Berlin) 28: 519, 1942.
330. Brett, C. H., The Journal of Economic Entomology 39: 677, 1946.
331. Brett, C. H., et al., Oklahoma Agricultural Experiment Station Bulletin No. 24, 1946.
332. Brett, C. H., and Brubaker, R. W., The Journal of Economic Entomology 48(3): 343, 1955.
333. Brett, C. H., and Eitel, W., The Journal of Economic Entomology 45: 346, 1952.
334. Brett, C. H., and Rhoades, W. C., The Journal of Economic Entomology 39: 677, 1946.
335. Ibid., 40: 572, 1947.
336. Brian, P., Journal of the Society of Chemical Industry (London) 64: 315, 1945.
337. Briejèr, C. J., Naamloze Vennootschap de Bataafsche Petroleum Maatschappij Laboratorium (Amsterdam), 1939, (Royal Dutch Petroleum Co., Ltd.).
338. Briejèr, C. J., Seventh International Congress of Entomology, Berlin 1938 IV p. 2753.
339. Briejèr, C. J., Nature (London) 141: 1099, 1938.
340. Bright, N. E. H., et al., Journal of the Science of Food and Agriculture 1: 344, 1950.

341. Brindley, T. A., and Chamberlin, J. C., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
342. Britton, W. E., Connecticut Agricultural Experiment Station Report No. 31, 1908.
343. Bromley, S. W., The Journal of Economic Entomology 40: 237, 1947.
344. Bronson, T. E., and Dudley, J. E., The Journal of Economic Entomology 33: 736, 1940.
345. Bronson, T. E., and Hall, S. A., Agricultural Chemicals 1(7): 19, 1946.
346. Bronson, T. E., and Stone, P. V., The Journal of Economic Entomology 42: 156, 1949.
347. Brooks, F. A., Agricultural Engineering (American Society of Agricultural Engineers) St. Joseph, Michigan 28: 233, 1947.
348. Brooks, T. S. and Dahm, R. A., The Journal of Economic Entomology 45(2): 349, 1952.
349. Brooks, W. J., and Anderson, L. D., The Journal of Economic Entomology 40: 220, 1947.
350. Brown, A. W. A., The Canadian Entomologist 79: 161, 1947.
351. Brown, A. W. A., Canadian Journal of Research 26: 177, 1948.
352. Brown, A. W. A., Contributed Data, 1955.
353. Brown, A. W. A., "Insect Control by Chemicals", John Wiley and Sons, New York, 1951.
354. Brown, A. W. A., The Journal of Economic Entomology 40: 607, 1947.
355. Ibid., 42: 399, 1949.
356. Brown, A. W. A., et al., Canadian Journal of Research D26: 188, 1948.
357. Brown, A. W. A., and Bishopp, F. C., Journal of the American Water Works Association 40: 264, 1948.
358. Brown, A. W. A., and Bishopp, F. C., Proceedings, 19th Annual Conference of the Maryland and Delaware Water and Sewage Association, 1946.
359. Brown, A. W. A., and Hurtig, H., The Journal of Economic Entomology 40: 276, 1947.
360. Brown, A. W. A., and Putnam, L. G., The Journal of Economic Entomology 39: 676, 1947.
361. Brown, H. V., and Bush, A. F., Archives of Industrial Hygiene and Occupational Medicine 1: 633, 1950.
362. Brown, H., and Rogers, E., Journal of the American Chemical Society 72: 1864, 1950.
363. Brown, J. H. U., Proceedings of the Society for Experimental Biology and Medicine 83: 59, 1953.
364. Brown, W. B., and Lewis, S. E., The Journal of the Society of Chemical Industry (London) 65: 241, 1946.
365. Browning, E., Medical Research Council Report No. 80, 1933.
366. Browning, H. S., et al., Canadian Journal of Research D26: 282, 1948.
367. Ibid., D26: 301, 1948.
368. Bruce, R. B., et al., Federation Proceedings 13: 339, 1954.
369. Bruce, R. B., et al., Journal of Agricultural and Food Chemistry 3(12): 1017, 1955.
370. Bruce, W. G., in "Insects", The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
371. Bruce, W. N., in "Insects", The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
372. Bruce, W. N., Pests and Their Control (Kansas City) 17: 7, 28, 1949.
373. Bruce, W. N., and Decker, G. C., Soap and Sanitary Chemicals 26(3): 123, 1950.
374. Ibid., 26(3): 122; 145, 1950.
375. Bruce, W. N., and Tauber, O. E., The Journal of Economic Entomology 38: 439, 1945.
376. Bruchhauser, F., and Gerhard, H., Berichte; Deutsche chemische Gesellschaft B72: 830, 1939.
377. Bruhin, J., Dissertation, Zurich, 1942; Deutsche Zeitschrift für die gesamte gerichtliche Medizin (Berlin) 37: A 253, 1943.
378. Brunn, K., and Allen, T. C., The Journal of Economic Entomology 38(3): 392, 1945.
379. Brussart, J. E., and Schor, A., Soap and Sanitary Chemicals 24: 126, 1948.
380. Bryson, M. J., et al., Advances in Chemistry Series 1: 232, 1950.
381. Buck, J. B., et al., Annals of the Entomological Society of America 45: 369, 1952.
382. Buck, J. B., and Boche, R. D., The Biological Bulletin 75: 344, 1938.
383. Buck, J. B., and Keister, M., The Biological Bulletin 97: 64, 1949.
384. Buckley, R., and Colthurst, J. P., The Analyst (London) 79: 285, 1954.
385. Budowski, P., et al., Journal of the American Oil Chemists' Society 28: 51, 1951.
386. Bugbee, J. W., et al., Sewage Works Journal 5: 567, 1933.
387. Bulger, J. W., The Journal of Economic Entomology 25(2): 261, 1932.
388. Bundren, J., et al., Proceedings of the Society for Experimental Biology and Medicine 79: 236, 1952.
389. Buntin, G., U.S. Patent No. 2, 565, 471 (1951).
390. Burden, G. S., and Cole, M. M., The Journal of Economic Entomology 49(5): 643, 1956.
391. Burgen, A. S. V., The British Journal of Pharmacology and Chemotherapy 4: 219, 1949.
392. Burgen, A. S. V., et al., The Journal of Pharmacology and Experimental Therapeutics 96: 396, 1949.
393. Burgen, A. S. V., et al., Lancet, 1948, p. 519.
394. Burgen, A. S. V., et al., Nature (London) 160: 760, 1947.
395. Burgen, A. S. V., and Hobbiger, F., The British Journal of Pharmacology and Chemotherapy 6: 593, 1951.
396. Burgess, R., Journal of the Society of Dyers and Colourists (Bradford, England) 51: 85, 1935.
397. Burgi, E., Bruxélles- medical 16: 1481, 1936.
398. Burlington, H., and Lindeman, V. F., Proceedings of the Society for Experimental Biology and Medicine 74: 48, 1950.
399. Burnet, I. M., and Holmes, E., Proceedings of the First International Congress of Plant Protection, Heverlee (The Netherlands) 1946, p. 295.
400. Burroughs, A. M., Proceedings. American Society for Horticultural Science (Geneva, New York) 25: 269, 1923.
401. Burtt, E., Annals of Applied Biology 32: 247, 1945.
402. Ibid., 32: 271, 1945.
403. Busbey, R. L., The Journal of Economic Entomology 35(3): 452, 1942.
404. Busbey, R. L., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine E-612, 1944.
405. Bushland, R. C., The Journal of Economic Entomology 33(4): 666, 1940.

406. Ibid., 33(4): 669, 1940.
407. Bushland, R. C., et al., The Journal of Economic Entomology 41: 642, 1948.
408. Ibid., 43: 649, 1950.
409. Bushland, R. C., et al., The Journal of Parasitology 30: 377, 1944.
410. Bushland, R. C., and King, W. V., U. S. Department of Agriculture Bulletin E-586, 1943.
411. Buston, H., et al., Nature (London) 158: 22, 1946.
412. Busvine, J. R., Annals of Applied Biology 25: 605, 1938.
413. Ibid., 33(3): 271, 1946.
414. Busvine, J. R., Bulletin of Entomological Research (London) 36: 23, 1945.
415. Busvine, J. R., Journal of the Society of Chemical Industry 65(11): 356, 1946.
416. Busvine, J. R., Nature (London) 150: 108, 1942.
417. Ibid., 150: 208, 1942.
418. Ibid., 156: 169, 1945.
419. Ibid., 158: 22, 1946.
420. Ibid., 168: 193, 1951.
421. Ibid., 171: 118, 1953.
422. Ibid., 174: 783, 1954.
423. Busvine, J. R., Transactions of the 9th International Congress of Entomology, Amsterdam 1951, Volume II, p. 335.
424. Busvine, J. R., and Buxton, P. A., The British Medical Journal No. 4240, 464, 1942.
425. Busvine, J. R., and Harrison, C. M., Bulletin of Entomological Research (London) 44: 729, 1953.
426. Busvine, J. R., and Kennedy, J. S. Annals of Applied Biology 36: 76, 1949.
427. Butler, C. G., et al., Annals of Applied Biology 30: 143, 1943.
428. Butler, E. C. B., et al., British Journal of Industrial Medicine 2: 30, 1945.
429. Butler, G. D., and Shaw, F. R., Gleanings in Bee Culture June, 1948, p. 348.
430. Butts, J., et al., Science 117: 699, 1953.
431. Butts, W. L., and Davidson, R. H., The Journal of Economic Entomology 48(5): 572, 1955.
432. Buxton, P. A., "The Louse". Edward Arnold, London, 1946.
433. Byers, G. W., et al., The Journal of Economic Entomology 49(4): 556, 1956.
434. Byers, H. G., U.S. Department of Agriculture Technical Bulletin No. 482, 1935.
435. Bynum, E. K., et al., The Journal of Economic Entomology 42: 556, 1949.
436. Caffrey, D. J., in "Insects", The Yearbook of Agriculture, 1952. U.S. Department of Agriculture, Washington, D.C.
437. Cahn, R., et al., Journal of the Society of Chemical Industry (London) 64: 33, 1945.
438. Cain, T. L., Proceedings of the Florida Anti-Mosquito Association 1950, p. 84.
439. Cakebread, E. J. N., Proceedings of the First International Congress of Plant Protection, Heverlee (The Netherlands) 1946.
440. Caldwell, N. E. H., The Queensland Agricultural Journal (Australia) 65: 53, 1947.
441. California Department of Health, Report.
442. Callaway, S., et al., Nature (London) 170: 843, 1952.
443. Callaway, S., et al., The British Medical Journal 2: 812, 1952.
444. Callaway, S., and Musgrave, A. J., Annals of Applied Biology 27: 252, 1940.
445. Callens, J. Y., General Report in Verhandelingen Eeerste International Congres voor Phytopharmacie, Heverlee (Nederlands) 1946.
446. Calvery, H. O., The Journal of the American Medical Association 111: 1722, 1938.
447. Camava, Archivio di scienze biologiche (Bologna) 24: 442, 1938.
448. Cameron, G. R., British Medical Bulletin 3: 233, 1945.
449. Cameron, G. R., et al., The Journal of Pathology and Bacteriology (London) 49: 363, 1939.
450. Cameron, G. R., and Burgess, F., The British Medical Journal 1: 865, 1945.
451. Cameron, G. R., and Burgess, F., British Ministry of Production; Insecticide Development Panel, Report No. 44, p. 131, 1944.
452. Cameron, G. R., and Cheng, K. K., The British Medical Journal 2: 819, 1951.
453. Campbell, A. M. G., Lancet 257: 1178, 1949.
454. Campbell, F. L., Journal of Agricultural Research (Washington, D.C.) 32: 359, 1926.
455. Campbell, F. L., The Journal of Economic Entomology 25(4): 905, 1932.
456. Campbell, F. L., The Journal of Pharmacology and Experimental Therapeutics 26: 277, 1926.
457. Campbell, F. L., et al., The Journal of Economic Entomology 26: 500, 1933.
458. Ibid., 27: 1176, 1934.
459. Campbell, F. L., and Filmer, R. S., Transactions of the Fourth International Congress of Entomology 1929, p. 523.
460. Campbell, F. L., and Lukens, C., The Journal of Economic Entomology 24: 88, 1931.
461. Campbell, F. L., and Sullivan, W. N., Soap and Sanitary Chemicals 14(6): 119, 1938.
462. Campbell, I., and Harper, S., Journal of the Chemical Society 1945, p. 283.
463. Campbell, I., and Harper, S., Journal of the Science of Food and Agriculture 3: 189, 1952.
464. Campbell, J. A., The Journal (Straits Branch) of the Royal Asiatic Society of Great Britain and Ireland 73: 129, 1916.
465. Campbell, R., The Journal of Economic Entomology 35: 26, 1942.
466. Cantarow, A., The Journal of Pharmacology and Experimental Therapeutics 63: 153, 1938.
467. Cardiff, I. D., The Journal of Industrial Hygiene and Toxicology 22: 333, 1940.
468. Carimini, M., Redia 28: 103, 1942.
469. Carlos-Suarez, C., et al., Analytical Chemistry 24: 668, 1952.
470. Carlson, E. C., et al., The Journal of Economic Entomology 40: 57, 1947.
471. Carlson, F. W., et al., The Journal of Economic Entomology 41: 655, 1948.
472. Carlson, F. W., and Newcomer, E. J., The Journal of Economic Entomology 42: 338, 1949.
473. Carman, G. E., The Journal of Economic Entomology 49(1): 103, 1956.
474. Carman, G. E., et al., The Journal of Economic Entomology 45: 767, 1952.
475. Carman, G. E., and Ewart, W. H., University of California Citrus Experiment Station Newsletter No. 48, 1950.
476. Carollo, J. A., Journal of the American Water Works Association 37: 1310, 1945.
477. Carpenter, C. P., The Journal of Industrial Hygiene and Toxicology 19: 323, 1937.
478. Carpenter, C. P., et al., Archives of Industrial Hygiene and Occupational Medicine 2: 420, 1950.
479. Ibid., 4: 261, 1951.
480. Carpenter, C. P., et al., The Journal of Industrial Hygiene and Toxicology 31: 343, 1949.

481. Carruth, L. A., The Journal of Economic Entomology 38(1): 59, 1945.
482. Carruth, L. A., and Howe, M. L., The Journal of Economic Entomology 41: 352, 1948.
483. Carter, J. W., The Journal of Economic Entomology 43: 677, 1950.
484. Carter, R. H., in "Insects", The Yearbook of Agriculture 1952. U.S. Department of Agricul ture, Washington, D.C.
485. Carter, R. H., The Journal of Economic Entomology 24: 263, 1931.
486. Carter, R. H., U.S. Department of Agriculture Bureau of Entomology and Plant Quarantine, Series E, 1937.
487. Carter, W., in "Insects", The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
488. Carter, W., The Journal of Economic Entomology 38(1); 35, 1945.
489. Ibid., 43: 677, 1950.
490. Ibid., 45(6): 981, 1952.
491. Carter, W., Science 97: 383, 1943.
492. Casida, J. E., et al., Journal of the American Chemical Society 74: 5548, 1952.
493. Casida, J. E., et al., The Journal of Biological Chemistry 210: 607, 1954.
494. Casida, J. E., et al., The Journal of Economic Entomology 45(4): 568, 1952.
495. Ibid., 47(1): 64, 1954.
496. Casida, J. E., et al., Nature (London) 172: 243, 1953.
497. Casida, J. E., and Stahmann, M. A., Journal of Agricultural and Food Chemistry 1(14): 883, 1953.
498. Cassaday, J. T., et al., Advances in Chemistry Series 1: 143, 1950.
499. Castagne, E., Compte Rendu; Premier Congrès international de phytopharmacie, Heverlee (Pays-Bas) 1946, p. 83.
500. Celice, J., et al., Le Bulletin médical (Paris) 66: 41, 1952.
501. Chabrolin, C., Comptes Rendus hebdomadaires des séances de l' Académie des sciences (Paris) 210: 262, 1940.
502. Chadbourne, D. S., and Rainwater, C. F., The Journal of Economic Entomology 46(1): 44, 1953.
503. Chadwick, L., et al., The Biological Bulletin 104: 323, 1953.
504. Ibid., 106: 139, 1954.
505. Chadwick, L., and Hill, D., Journal of Neurophysiology 10: 235, 1947.
506. Chaix, P., et al., Biochimica et Biophysica Acta 2: 57, 1948.
507. Ibid., 2: 86, 1948.
508. Chamberlain, R., The American Journal of Hygiene 52: 153, 1950.
509. Chamberlain, W. F., and Hoskins, W. M., The Journal of Economic Entomology 44(2): 177, 1951.
510. Chamberlin, F. S., The Journal of Economic Entomology 42: 544, 1949.
511. Chamberlin, T. R., et al., The Journal of Economic Entomology 41: 509, 1948.
512. Chamberlin, T. R., and Medler, J. T., The Journal of Economic Entomology 42: 653, 1949.
513. Chambers, W. H., et al., U.S. Army Chemical Corps, Medical Division Research Report No. 23, October, 1950.
514. Chandler, S. C., The Journal of Economic Entomology 39: 666, 1946.
515. Ibid., 41: 52, 1948.
516. Ibid., 42: 514, 1949.
517. Ibid., 43: 73, 1950.
518. Chandler, S. C., Transactions of the Illinois Horticultural Society 79: 274, 1945.
519. Chang, P., Annals of the Entomological Society of America 44: 311, 1951.
520. Chang, S. C., The Journal of Economic Entomology 45(3): 370, 1952.
521. Chao, Y.-C., and DeLong, M., The Journal of Economic Entomology 46(5): 908, 1953.
522. Chapman, N., and Saunders, B., Journal of the Chemical Society 1948, p. 1010.
523. Chapman, P. J., et al., in "Insects", The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
524. Chapman, P. J., et al., The Journal of Economic Entomology 36: 241, 1943.
525. Chapman, P. J., and Avens, A. W., The Journal of Economic Entomology 41(2): 190, 1948.
526. Chapman, P. J., and Lienk, S. E., The Journal of Economic Entomology 43: 309, 1950.
527. Chappellier, A., and Raucourt, M., Annales des épiphyties et de phytogénétique (now Annales des épiphyties) (Paris) (Institut national de la recherche agronomique). 8(1): 1, 1945.
528. Chargaff, E., et al., Science 108: 556, 1948.
529. Chaudhuri, R. N., and Mukerji, A. K., The Indian Medical Gazette (Calcutta) 82: 115, 1947.
530. Chen, Proceedings of the Society for Experimental Biology and Medicine 38: 241, 1938.
531. Cheng, K., The British Journal of Experimental Pathology 32: 444, 1951.
532. Cheng, T. H., and Campbell, F. L., The Journal of Economic Entomology 33: 193, 1940.
533. Chennels, M., et al., The Journal of Physiology (London) 108: 375, 1949.
534. Cherfuka, W., and Smallman, B., Nature (London) 175: 946, 1955.
535. Cherian, M. C., and Mahadevan, V., Indian Bee Journal 8: 128, 1946.
536. Chevalier, J., Bulletin des sciences pharmacologiques (Paris) 37: 154, 1930.
537. Chilean Nitrate Educational Bureau, "Bibliography of Literature on Minor Elements", 4th Edition, Volume I, 1948.
538. Chipman, W. A., and Galtsoff, P. S., U.S. Department of the Interior Special Scientific Report, Fisheries No. 1, August, 1949.
539. Chisholm, R. D., in "Insects", The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
540. Chisholm, R. D., U.S. Department of Agriculture Bulletin No. E-643, 1945.
541. Chittenden, F. H., U.S. Department of Agriculture Farmer's Bulletin No. 45, 1896.
542. Chopra, R. N., and Badhwar, R. L., Indian Journal of Agricultural Science 10: 1, 1940.
543. Christ, E. G., and Driggers, B. F., The Journal of Economic Entomology 42: 559, 1949.
544. Christensen, B. V., and Lynch, H. J., The Journal of Pharmacology and Experimental Therapeutics 48: 311, 1933.
545. Christiani, H., and Chausse, M., Comptes rendus des séances de la Societé de biologie (Paris) 96: 843, 1927.
546. Claborn, H. V., et al., Agricultural Chemicals 8: 37, 1953.
547. Clark, B. M., South African Medical Journal (Capetown) 20: 518, 1946.

548. Clark, E. L., et al., Journal of Agricultural and Food Chemistry 3(10): 834, 1955.
549. Clarke, C. A., et al., British Journal of Industrial Medicine 2: 17, 1945.
550. Clausen, C. P., Annals of the Entomological Society of America 29: 201, 1936.
551. Clausen, R. L., Verhandlungen der Naturforschenden Gesellschaft in Basel (Switzerland) 127: 93, 1947.
552. Clausen, R. L., and Günthart, E., Proceedings of the First International Congress of Plant Protection, Heverlee (The Netherlands) 1946, p. 289.
553. Clower, D. F., and Matthysse, J. G., The Journal of Economic Entomology 47(5): 735, 1954.
554. Coates, H., Annals of Applied Biology 36: 156, 1949.
555. Coates, H., Nature (London) 163: 497, 1949.
556. Cobey, F. A., et al., Science 123: 140, 1956.
557. Coburn, D. R., and Treichler, R., Journal of Wildlife Management 10: 208, 1946.
558. Cochran, D. G., The Journal of Economic Entomology 48(2): 131, 1955.
559. Ibid., 49(1): 43, 1956.
560. Cochran, J. H., The Journal of Economic Entomology 42: 348, 1949.
561. Cockerham, K. L., and Dean, O. T., The Journal of Economic Entomology 41: 563, 1948.
562. Cohen, J. A., et al., The Journal of Clinical Investigation 33: 459, 1954.
563. Cohen, W. D., Recueil des travaux chimiques des Pays-Bas (et de la Belgique) (Amsterdam) 57(6): 653, 1938.
564. Cole, A. E., "Effects of Pollutional Wastes on Fish", A Symposium on Hydrobiology, University of Wisconsin 1941, p. 215.
565. Cole, C. E., and Fisk, F. W., The Journal of Economic Entomology 48(1): 85, 1955.
566. Cole, M. M., and Burden, G. S., The Journal of Economic Entomology 49(6): 747, 1956.
567. Cole, M. M., and Lloyd, G. W., The Journal of Economic Entomology 44(6): 1025, 1951.
568. Collias, E., et al., The Journal of Cellular and Comparative Physiology 40: 507, 1952.
569. Collier, H., Canadian Journal of Research 18B: 345, 1940.
570. Collier, H., Lancet, 1936, p. 594.
571. Collier, H., and Allen, D., Canadian Journal of Research 20B: 189, 1942.
572. Collier, H., and Allen D., The Journal of Biological Chemistry 140: 675, 1941.
573. Collins, D. L., The Journal of Economic Entomology 27: 379, 1934.
574. Commercial Solvents Corporation, Technical Bulletins 1 and 2, 1949.
575. Ibid., Technical Bulletin, 1951.
576. Committee on Pesticides, The Journal of the American Medical Association 145(10): 728, 1951.
577. Compton, C. C., Illinois Agricultural Experiment Station Circular No. 391, 1932.
578. Conklin, J. G., and Walker, G. L., The Journal of Economic Entomology 42: 153, 1949.
579. Conley, B. E., The Journal of the American Medical Association 144: 104, 1950.
580. Ibid., 145: 728, 1950.
581. Ibid., 147: 571, 1951.
582. Ibid., 149: 367, 1952.
583. Ibid., 149: 1135, 1952.
584. Ibid., 152: 1232, 1953.
585. Cook, A. J., Michigan Agricultural Experiment Station Bulletin No. 59, 1890.
586. Cook, F. C., U.S. Department of Agriculture Bulletin No. 1147, 1923.
587. Cook, H., et al., Journal of the Chemical Society 1949, p. 635.
588. Coon, B. F., The Journal of Economic Entomology 37: 785, 1944.
589. Coon, J. M., and Salerno, P. R., Federation Proceedings 7: 212, 1948.
590. Cooper, H. P., et al., South Carolina Agricultural Experiment Station Annual Report No. 44, 1931, p. 28.
591. Ibid., Report No. 45, 1932.
592. Cooper, W. F., and Nuttall, W. H., Annals of Applied Biology 1: 273, 1915.
593. Cooper, W. F., and Walling, W. A. B., Annals of Applied Biology 2: 166, 1915-1916.
594. Cope, O. B., in "Insects", The Yearbook of Agriculture, 1952. U. S. Department of Agriculture, Washington, D.C.
595. Cope, O. B., et al., Transactions. The American Fisheries Society 77: 160, 1947.
596. Coper, H., et al., Archiv fur experimentelle Pathologie und Pharmakologie (Leipzig) 212: 463, 1951.
597. Coper, H., et al., Klinische Wochenschrift (Berlin) 30: 551, 1952.
598. Corcoran, A. N., A Paper Presented to the Michigan Sewage Works Association at Traverse City, Michigan May 25, 1949.
599. Corey, R. A., et al., The Journal of Economic Entomology 46(2): 386, 1953.
600. Corey, R. A., et al., Science 118: 28, 1953.
601. Corteggiani, E., and Serfaty, A., Comptes rendus des séances de la Societé de biologie (Paris) 131: 1124, 1939.
602. Cory, E. N., and Langford, G. S., The Journal of Economic Entomology 40: 425, 1947.
603. Cottam, C., Address to the American Association of Economic Entomologists at New York, December, 1948. Quoted by Brown, A. W. A.
604. Cottam, C., and Higgins, E., The Journal of Economic Entomology 39: 44, 1946.
605. Cotton, R. T., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
606. Cotton, R. T., "Insect Pests of Stored Grain and Grain Products." Burgess, 1941.
607. Cotton, R. T., The Journal of Economic Entomology 23: 231, 1930.
608. Ibid., 25: 1088, 1932.
609. Ibid., 37(3): 380, 1944.
610. Cotton, R. T., et al., U.S. Department of Agriculture Circular No. 720, 1945.
611. Cotton, R. T., and Ashby, W., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
612. Cotton, R. T., and Roark, R. C., Industrial and Engineering Chemistry 20: 380, 1928.
613. Ibid., 20: 805, 1928.
614. Cotton, R. T., and Roark, R. C., The Journal of Economic Entomology 20: 636, 1928.
615. Cotton, R. T., and Walkden, H. H., The Journal of Economic Entomology 39(4): 529, 1946.
616. Cotton, R. T., and Young, H. D., The Journal of Economic Entomology 36(1): 116, 1943.
617. Cotton, R. T., and Young, H. D., Proceedings of the Entomological Society of Washington 31: 97, 1929.
618. Coury, T., and Ranzoni, G., Biological Abstracts 21, item 18: 273, 1947.

619. Cox A. J., Agricultural Chemicals 2(1): 22, 1947.
620. Ibid., 2(2); 29, 1947.
621. Cox, A. J., and Rodgerson, E. B , Proceedings of the Society for Experimental Biology and Medicine 32: 653, 1935.
622. Cox, H. C., et al., The Journal of Economic Entomology 49(1): 113, 1956.
623. Cox, J. A., The Journal of Economic Entomology 40: 195, 1947.
624. Ibid., 42: 507, 1949.
625. Ibid., 42: 702, 1949.
626. Cox, J. A., and Daniel, D. M., The Journal of Economic Entomology 28: 113, 1935.
627. Coyer, H. A., Industrial Medicine 13: 230, 1944.
628. Crabtree, D. G., Soap and Sanitary Chemicals 26(2): 131, 1950.
629. Crafts, A. S., Science 101: 417, 1945.
630. Crafts, A. S., and Rieber, H. G., Hilgardia 18: 77, 1948.
631. Crafts, A. S., and Rosenfels, R. S., Hilgardia 12: 177, 1939.
632. Craig, L. C., Iowa State College Journal of Science 5: 327, 1931.
633. Craig, L. C., Journal of the American Chemical Society 55: 2543, 1933.
634. Craig, L. C., and Richardson, C. H., Iowa State College Journal of Science 7: 477, 1933.
635. Cranham, J. E., et al., Chemistry and Industry No. 45 (November 7) p. 1206, 1953.
636. Craufurd-Benson, H. J., British Medical Bulletin 3: 224, 1945.
637. Craufurd-Benson, H. J., Bulletin of Entomological Research (London) 29: 41, 1938.
638. Creighton, J. T., The Journal of Economic Entomology 31(6): 745, 1938.
639. Creighton, J. T., and Gresham, W. B., The Journal of Economic Entomology 40(6): 915, 1947.
640. Crescitelli, F., and Gilman, A., The American Journal of Physiology 147: 127, 1946.
641. Crescitelli, Y., Dissertation, Würzburg, 1933.
642. Cristol, S. J., Advances in Chemistry Series 1: 184, 1950.
643. Cristol, S. J., Journal of the American Chemical Society 67: 1494, 1945.
644. Ibid., 69: 338, 1947.
645. Cristol, S. J., et al., Journal of the American Chemical Society 74: 3333, 1952.
646. Cristol, S. J., et al., Science 104: 343, 1946.
647. Cristol, S. J., and Haller, H. L., Journal of the American Chemical Society 70: 1323, 1948.
648. Cristol, S. J., and Harms, D., Journal of the American Chemical Society 71: 2875, 1949.
649. Crofts, P. C., Reports on the Progress of Applied Chemistry XXXV, 328, 1950.
650. Croland, R., Annales de physiologie et de physicochimie biologique (Paris) 13: 294, 1937.
651. Crombie, L., et al., Journal of the Chemical Society 1950, p. 3552.
652. Ibid., 1951, p. 2906.
653. Crombie, L., and Harper, S. H., Journal of the Chemical Society 1950, p. 1152.
654. Crombie, L., and Harper, S. H., Nature (London) 164: 534, 1949.
655. Ibid., 164: 1053, 1949.
656. Cross, H. F., and Snyder, F. M., The Journal of Economic Entomology 41: 936, 1948.
657. Cross, R. J., et al., The Journal of Biological Chemistry 177: 655, 1949.
658. Crow, J. F., The Journal of Economic Entomology 47: 393, 1954.
659. Crowell, H. H., et al., The Journal of Economic Entomology 41: 362, 1948.
660. Crowell, H. H., and Morrison, H. E., The Journal of Economic Entomology 43(1): 14, 1950.
661. Crumb, S. E., and Chamberlin, F. S., The Journal of Economic Entomology 29(5): 983, 1936.
662. Cullinan, F. P., Agricultural Chemicals 2(5): 18, 1947.
663. Cullinan, F. P., The Journal of Economic Entomology 42: 387, 1949.
664. Culver, D., Stanford Medical Bulletin (San Francisco) 8: 112, 1950.
665. Cunningham, G. H., "Plant Protection by Aid of Therapeutics", Dunedin (New Zealand), John McIndoc, 1935.
666. Cunningham, H. B., and Eden, W. G., The Journal of Economic Entomology 48(1): 109, 1955.
667. Cunningham, R. E., and Hill, F. S., Pediatrics (U.S.) 9: 745, 1952.
668. Cupples, H. L., Journal of the American Chemical Society 72: 4522, 1950.
669. Cupples, H. L., et al., The Journal of Economic Entomology 29(3): 611, 1936.
670. Curl, L. F., and White R. W., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
671. Cutkomp, L. K., The Journal of Economic Entomology 40(2): 328, 1947.
672. Ibid., 44(6): 898, 1951.
673. Cutkomp, L. K., The Journal of Pharmacology and Experimental Therapeutics 77: 238, 1943.
674. Cutkomp, L. K., Soap and Sanitary Chemicals 19(10): 107, 1943.
675. Cutkomp, W. A., and Holdaway, F. G., The Journal of Economic Entomology 43: 433, 1950.
676. Cutright, C. R., and Parks, T. H., The Journal of Economic Entomology 42: 359, 1949.
677. Cutright, C. R., and Sutton, R., The Journal of Economic Entomology 40: 557, 1947.
678. Czensny, R., Abhandlungen aus der Fischerei und derer Hilfswissenschaften 2: 233, 1950.
679. Dahlen, J. H., and Haugen, A. O., Journal of Wildlife Management 18: 477, 1954.
680. Dahm, P. A., The Journal of Economic Entomology 45: 763, 1952.
681. Dahm, P. A., et al., Journal of Dairy Science 33: 747, 1950.
682. Dahm, P. A., et al., Science 112: 254, 1950.
683. Dahms, R. G., The Journal of Economic Entomology 41: 520, 1948.
684. D'Alessandro, G., et al., Sicilia medica (Palermo) 6: 5, 1949.
685. Dallemagne, M. J., Revue médicale de Liége (Belgique) 7: 356, 1952.
686. Dallemagne, M. J., et al., Science 112: 148, 1950.
687. Dallemagne, M. J., and Phillipot, E., Archives internationales de pharmacodynamie et de thérapie (Paris) 76: 274, 1948.
688. Dalton, F., and Hurwitz, C., Soil Science 66: 233, 1948.
689. Dauben, H., and Wenkert, E., Journal of the American Chemical Society 69: 2074, 1947.
690. Daugherty, F. M., and Garrett, J. T., Texas Journal of Science 3: 391, 1951 (Water Pollution Abstracts 26: 49, 1953.)
691. Davenport, V., Physiological Zoölogy 22: 35, 1949.
692. David, D. R., Proceedings of the Royal Society of Medicine 45: 570, 1952.

693. David, W. A. L., Annals of Applied Biology 33(2): 133, 1946.
694. Ibid., 38: 508, 1951.
695. Ibid., 39: 203, 1952.
696. David, W. A. L., Ministry of Production (Great Britain), Insecticide Development Panel Report No. 45, p. 236, 1945.
697. David, W. A. L., Bulletin of Entomological Research (London) 35: 101, 1944.
698. David, W. A. L., Nature (London) 166: 72, 1950.
699. David, W. A. L., and Bracey P., Bulletin of Entomological Research (London) 37: 393, 1947.
700. David, W. A. L., and Bracey, P., Nature (London) 153: 594, 1944.
701. David, W. A. L., and Gardiner, B. O. C., Annals of Applied Biology 38: 91, 1951.
702. Ibid., 40: 91, 1953.
703. Ibid., 40: 403, 1953.
704. Ibid., 41: 261, 1954.
705. David, W. A. L., and Kilby, B., Nature (London) 164: 522, 1949.
706. Davidov, B., et al., Federation Proceedings 10: 291, 1951.
707. Davidov, B., et al., Science 118: 383, 1953.
708. Davidov, B., and Frawley, J. P., Proceedings of the Society for Experimental Biology and Medicine 76: 780, 1951.
709. Davidov, B., and Radomski, J. L., The Journal of Pharmacology and Experimental Therapeutics 107: 259, 1953.
710. Ibid., 107: 266, 1953.
711. Davidson, W. H., The Journal of Economic Entomology 23: 868, 1930.
712. Ibid., 23: 877, 1930.
713. Davies, D. R., The Journal of Pharmacy and Pharmacology (London) 6: 1, 1954.
714. Davies, D. R., Proceedings of the Royal Society of Medicine 45: 570, 1952.
715. Davies, D. R., et al., Biochemical Journal (London) 53: xv, 1953.
716. Davies, D. R., and Rutland, A., Biochemical Journal (London) 47: xxii, 1950.
717. Davies, N., and Dick, J. H., Journal of the Chemical Society 1932, p. 483.
718. Davis, A. C., and Swenson, K. G., The Journal of Economic Entomology 46: 321, 1953.
719. Davis, D. W., and Sessions, A. C., The Journal of Economic Entomology 46: 526, 1953.
720. Davison, Proceedings of the 317th Meeting of the Biochemical Society, 1953.
721. Dawson, E. H., et al., Journal of Agricultural and Food Chemistry 1(5): 399, 1953.
722. Dawson, J., and Croxall, W., U.S. Patents 2,562,893 and 2,588,215, (1951; 1952.)
723. Dawson, R. B., and Escritt, J. R., Nature (London) 158: 448, 1946.
724. Dayrit, C., et al., The Journal of Pharmacology and Experimental Therapeutics 92: 173, 1948.
725. Dayus, C. V., The New Zealand Journal of Science and Technology B54: 170, 1937.
726. Dean, F. P., et al., The Journal of Economic Entomology 39: 523, 1946.
727. Dean, F. P., and Newcomer, E. J., The Journal of Economic Entomology 45(6): 1038, 1952.
728. Dean, H. T., Public Health Reports (Washington D.C.) 49: 1075, 1934.
729. Dean, R. W., and Chapman, P. J., New York State Agricultural Experiment Station Bulletin No. 716 1946.
730. Dearborn, F. E., The Journal of Economic Entomology 28: 710, 1935.
731. Ibid., 29: 445, 1936.
732. Ibid., 30: 140, 1937.
733. Ibid., 30: 958, 1937.
734. DeBach, P., et al., California Citrograph 40: 254, 1955.
735. Decker, G. C., et al., The Journal of Economic Entomology 40: 395, 1947.
736. Decker, G. C., and Bruce, W. N., The American Journal of Tropical Medicine 1: 395, 1952.
737. Decker, G. C., and Bruce, W. N., Bulletin of the National Research Council (U.S.) No. 219, 1952, p. 25.
738. De Eds, F., Medicine (Baltimore) 12: 1, 1933.
739. De Eds, F., and Eddy, C., Journal of the American Chemical Society 60: 1446, 1938.
740. De Eds, F., and Thomas, J., The Journal of Parasitology 27: 143, 1941.
741. De Francolini, J., Revue de pathologie végétale et d'entomologie agricole (Paris) 22: 39, 1935.
742. Deichmann, W. B., Annals of Internal Medicine 21: 803, 1944.
743. Deichmann, W. B., Chemagro Corporation, Technical Report, 1951.
744. Deichmann, W. B., Federation Proceedings 6: 322, 1947.
745. Ibid., 13: 346, 1954.
746. Deichmann, W. B., et al., Archives of Industrial Hygiene and Occupational Medicine 5: 44, 1952.
747. Deichmann, W. B., et al., The Journal of Pharmacology and Experimental Therapeutics 76: 104, 1942.
748. Deichmann, W. B., and Lampe, K., Bulletin of the Jackson Memorial Hospital, Miami, Florida (in press).
749. Deichmann, W. B., and Rakoczy, R., Archives of Industrial Hygiene and Occupational Medicine 7: 152, 1953.
750. Deichmann, W. B., and Witherup, S., Federation Proceedings 6: 322, 1947.
751. Del Canizo, J., and Urquijo, P., Boletin de patologia végetal y entomología agrícola (Madrid) 14: 181, 1946.
752. Del Guercio, G., Nuove Relazione della Reale Stazione d' Entomologia e d' Agricoltura (Firenze, Italia) 1: 124, 1900.
753. De Long, D. M., et al., Proceedings of the Ohio Vegetable and Potato Growers Association 24: 86, 1939.
754. Demyanenko, V., Chemical Abstracts 27: 2746, 1931.
755. Denninger, C., and Dumont, L., Compte Rendu; III^e Congrès international de phytopharmacie, Paris 1952, p. 310.
756. Denz, F. A., The Journal of Pathology and Bacteriology (London) 63: 81, 1951.
757. De Ong, E. R., "Chemistry and Uses of Insecticides" Reinhold, New York, 1948.
758. De Ong, E. R., The Journal of Economic Entomology 16: 486, 1923.
759. De Ong, E. R., et al., Hilgardia 2: 351, 1927.
760. Deonier, C. C., The Journal of Economic Entomology 31: 742, 1938.
761. Deonier, C. C., et al., The Journal of Economic Entomology 38(2): 241; 244, 1945.
762. Ibid., 39(4): 459, 1946.
763. Ibid., 43: 506, 1950.
764. Deonier, C. C., et al., Mosquito News 9: 150, 1949.
765. Ibid., 10: 138, 1950.

766. Deonier, C. C., et al., Science 103: 13, 1946.
767. Deonier, C. C., et al., Soap and Sanitary Chemicals 22(11): 118, 1946.
768. Deonier, C. C., and Lindquist, A. W., The Journal of Economic Entomology 35(5): 788, 1942.
769. Ibid., 36(1): 54, 1943.
770. Derbes, V. J., et al., The Journal of the American Medical Association 158: 1367, 1955.
771. Dérobert, L., et al., Annales de médecine légale (Paris) 30: 32, 1950.
772. Dervillée, P., et al., Report of the 8th International Congress for Industrial Accidents and Occupational Diseases, Frankfort am Main, Volume II, p. 903, 1939.
773. Desoille, H., et al., Archives des maladies professionelles; hygiène et toxicologie industrielles (Paris) 12: 389, 1951.
774. Dethier, V. G., Annual Review of Entomology 1: 181, 1956.
775. Detroux, I. L., Compte Rendu; III^{e} Congrès international de phytopharmacie, Paris 1952, p. 318.
776. Ibid., p. 324.
777. Dewey, J., The Journal of Economic Entomology 35(2): 256, 1942.
778. Dewey, J., and Van Geluwe, J. D., The Journal of Economic Entomology 41: 235, 1948.
779. Dewey, R. H., Data contributed on behalf of the Commercial Solvents Corporation in February, 1956.
780. DeWitt, J. B., Journal of Agricultural and Food Chemistry 3: 672, 1955.
781. DeWitt, J. B., Paper read before the Division of Food and Agricultural Chemistry, American Chemical Society, September 13, 1955.
782. DeWitt, J. B., et al., Journal of the American Pharmaceutical Association 44: 22, 1945.
783. Dibble, C. B., The Journal of Economic Entomology 26: 893, 1933.
784. Dicke, R. J., Thesis. University of Wisconsin, 1943.
785. Dicke, R. J., et al., The Journal of Economic Entomology 38(3): 389, 1945.
786. Dicker, G. H. L., et al., Journal of Pomology 22: 162, 1946.
787. Dickinson, B. C., et al., The Journal of Economic Entomology 34(5): 656, 1941.
788. Dickinson, D. G., The Journal of Economic Entomology 43: 557, 1950.
789. Dickson, R. C., Hilgardia 13: 515, 1941.
790. Dieke, S. H., and Richter, C. P., Public Health Reports (Washington, D.C.) 61: 672, 1946.
791. Diephuis, F., and Dunn, C. L., Montana Agricultural Experiment Station Bulletin No. 461, 1949.
792. Dierick, G.F.E.M., Tijdschrift over Plantenziekten (Amsterdam. Phytopathologisch Laboratorium "Willie Commelin Scholten") 49: 22, 1943.
793. Diggle, W. M., and Gage, J. C., Biochemical Journal (London) 48: xxv, 1951.
794. Ibid., 49: 491, 1951.
795. Diggle, W. M., and Gage, J. C., Nature (London) 168: 998, 1951.
796. Dills, L. E., and Odland, M. L., The Journal of Economic Entomology 41(6): 948, 1948.
797. DiStefano, V., and Hurwitz, L., Archives of Biochemistry and Biophysics 47: 228, 1953.
798. Ditman, L. P., et al., The Journal of Economic Entomology 33: 477, 1940.
799. Ibid., 38(2): 183, 1945.
800. Ditman, L. P., and Burkhardt, G., The Journal of Economic Entomology 45: 880, 1952.
801. Ditman, L. P., and Cory, E. N., The Journal of Economic Entomology 41: 268, 1948.
802. Division of Pharmacology, U.S. Food and Drug Administration, Report No. 7, March, 1938.
803. Ibid., Report No. 4, October, 1945.
804. Ibid., Quarterly Report No. 2, 1946.
805. Ibid., Quarterly Report No. 3, 1946.
806. Ibid., Report, September 1946.
807. Ibid., Quarterly Report No. 3, 1947.
808. Ibid., Report No. 4, 1947.
809. Ibid., Report No. 9, March 1948.
810. Dixon, W. E., Proceedings of the Royal Society of Medicine 20: 77, 1927.
811. Dobbins, T. N., The Journal of Economic Entomology 41: 815, 1948.
812. Dobroscky, I. D., The Journal of Economic Entomology 28: 627, 1935.
813. Dodds, E. C., and Robertson, J. D., 225: 1137, 1933.
814. Dodonov, B. A., "On the Comparative Resistance of Certain Insect Species to Arsenic and Fluorine Insecticides" (in Russian; Library of Congress) Leningrad Institut. Trudy po zashchite rasteniĭ Series III No. 7 pp. 55-75, 1936 (Plant Protection. U.S.S.R.).
815. Dogger, J. R., and Lilly, J. H., The Journal of Economic Entomology 42: 663, 1949.
816. Doisy, E. A., and Bocklage, B. C., Proceedings of the Society for Experimental Biology and Medicine 71: 490, 1949.
817. Ibid., 74: 613, 1950.
818. Domenjoz, R., Archives internationales de pharmacodynamie et de thérapie (Paris) 73: 128, 1946.
819. Domenjoz, R., Helvetica chimica acta (Basel) 29: 1317, 1946.
820. Dominick, C. B., The Journal of Economic Entomology 42(1): 148, 1949.
821. Ibid., 43(2): 221, 1950.
822. Ibid., 43(3): 295, 1950.
823. Donohoe, H. C., et al., The Journal of Economic Entomology 33(2): 296, 1940.
824. Donohue, E. L., Pests, July 1948.
825. Dormal, S., et al., The Journal of Economic Entomology 45(1): 73, 1952.
826. Dorward, K., Florida Entomology 31: 116, 1948.
827. Doudoroff, P., et al., U.S. Public Health Service Environmental Health Center Report No. 7, 1951 p. 13.
828. Doudoroff, P., et al., Sewage and Industrial Wastes 25: 840, 1953.
829. Douglass, J. R., and Shirk, F. H., The Journal of Economic Entomology 42(1): 68, 1949.
830. Doull, J., and Du Bois, K. P., The Journal of Pharmacology and Experimental Therapeutics 106: 382, 1952.
831. Dove, W. E., The American Journal of Tropical Medicine 27: 339, 1947.
832. Dove, W. E., U.S. Department of Agriculture Bulletin No. E-673, 1945.
833. Dove, W. E., and Schroeder, H. O., Journal of Agricultural and Food Chemistry 3(11): 932, 1955.
834. Dow Chemical Company, "Methyl Bromide for Mill and Warehouse Fumigation", 1945.
835. Dow Chemical Company, Technical Agricultural Bulletin No. 4, 1947.
836. Dow Chemical Company, Technical Bulletin, 1951.
837. Dowden, P. B., Report; Forest Insect Investigation, Department of Agriculture, Canada 2, No. 1
838. Dowdy, A. C., and Sleesman, J. P., The Journal of Economic Entomology 45(4): 640, 1952.

839. Draize, J. H., et al., Chemical and Engineering News 22: 1503, 1944.
840. Draize, J. H., et al., The Journal of Pharmacology and Experimental Therapeutics 82: 159, 1944.
841. Ibid., 82: 377, 1944.
842. Ibid., 93: 26, 1948.
843. Drake, N. L., and Spies, J. R., The Journal of Economic Entomology 25: 129, 1932.
844. Dratschew, S. M., Zeitschrift für Pflanzenernährung, Dungung und Bodenkunde (wissenschaftlicher Teil) (Berlin, Leipzig) A30: 156, 1933.
845. Dresden, D., Nature (London) 162: 1000, 1948.
846. Dresden, D., and Krijgsman, B., Bulletin of Entomological Research (London) 38: 575, 1948.
847. Dresden, D., and Openoorth, F., Bulletin of Entomological Research (London) 43: 581, 1953.
848. Driggers, B. F., and Darley, M. M., The Journal of Economic Entomology 42: 330, 1949.
849. Driggers, B. F., and O'Neil, W. J., The Journal of Economic Entomology 31: 221, 1938.
850. Driggers, B. F., and Pepper, B. B., The Journal of Economic Entomology 29: 447, 1936.
851. Drill, V. A., "Pharmacology in Medicine", McGraw-Hill, 1954.
852. DuBois, K. P., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, Volume II, p. 313.
853. DuBois, K. P., University of Chicago Toxicity Laboratory Reports, New Series, 20 - 22, 1948.
854. DuBois, K. P., et al., Archives of Industrial Hygiene and Occupational Medicine 8: 350, 1953.
855. DuBois, K. P., et al., Federation Proceedings 7: 216, 1948.
856. Ibid., 9: 269, 1950.
857. DuBois, K. P., et al., The Journal of Pharmacology and Experimental Therapeutics 95: 79, 1949.
858. Ibid., 97: 261, 1950.
859. Ibid., 98: 6, 1950.
860. Ibid., 99: 376, 1950.
861. DuBois, K. P., and Coon, M. J., Archives of Industrial Hygiene and Occupational Medicine 6: 9, 1955.
862. DuBois, K. P., and Cotter, C. J., American Medical Association Archives of Industrial Health 11: 53, 1955.
863. DuBois, K. P., and Doull, J., Federation Proceedings 9: 269, 1950.
864. DuBois, K. P., and Mangun, G. H., Proceedings of the Society for Experimental Biology and Medicine 64: 137, 1947.
865. Dubois, R., and Roux, L., Comptes rendus hebdomadaires des séances de l'Académie des sciences (Paris) 104: 1869, 1887.
866. Dudley, H. C., and Neal, P. A., Journal of Industrial Hygiene and Toxicology 24: 27, 1942.
867. Dudley, J. L., and Kammer, A. G., The Journal of the American Medical Association 153: 723, 1953.
868. Dudley, S. F., et al., The Journal of Industrial Hygiene and Toxicology 24: 255, 1943.
869. Ibid., 25: 13, 1943.
870. Dunavan, D., 58th Annual Report, South Carolina Agricultural Experiment Station, 1944-1945.
871. Dunn, E., et al., Nature (London) 158: 587, 1946.
872. Dunn, J. E., et al., Public Health Reports (Washington, D.C.) 61: 1614, 1946.
873. Dupire, A., and Raucourt, M., Comptes rendus hebdomadaires des séances de l'Académie d'Agriculture de France (Ministère d'Agriculture) 29: 470, 1943.
874. DuPont de Nemours (E.I.) Company "EPN: Manual of Technical Data", 2nd Edition, 1951.
875. DuPont de Nemours (E.I.) Company, "Methoxychlor: A Summary of Data on Toxicology". October, 1949.
876. DuPont de Nemours (E.I.) Company, "Residue Tolerance Status: Methoxychlor", Issue No. 1, February, 1956.
877. Durand-Gasselin, L., Agriculture 14: 115, 1950.
878. Duspiva, F., Mitteilungen aus der biologischen Zentralanstalt (Reichsanstalt) für Land- und Forst-wirtschaft (Berlin - Dahlem) No. 70, 1951 pp. 91 - 93 (February) (Pflanzenschutz-Tagung der biologischen Bundesanstalt, Braunschweig in Goslar pp. 11 - 14, October 1950.)
879. Dustan, A. G., The Canadian Entomologist 79: 1, 1947.
880. Dustan, A. G., Department of Agriculture, Canada, Division of Entomology, Proceedings, No. 89, 1948.
881. Dutton, W. C., The Journal of Economic Entomology 29(1): 62, 1936.
882. Dutton, W. C., Michigan Agricultural Experiment Station Bulletin No. 218, 1932.
883. Dutra, F., U.S. Food and Drug Administration Hearings, Exhibits 1215, 1281, (1950).
884. Duvoir, M., et al., Bulletin des sciences pharmacologiques (Paris) 46: 15, 1939.
885. Dybing, F., and Dybing, O., Acta pharmacologica et toxicologica (København) 2: 223, 1946.
886. Eagle, H., et al., The Journal of Clinical Investigation 25: 451, 1946.
887. Eagleson, C., The Journal of Economic Entomology 31(6): 778, 1938.
888. Eagleson, C., Soap and Sanitary Chemicals 16(1): 96, 1940.
889. Ibid., 17(5): 101, 1941.
890. Ibid., 18(12): 115, 1942.
891. Ibid., 18(12): 125, 1942.
892. Earl, Thompson, British Journal of Pharmacology and Chemotherapy 7: 261, 1952.
893. Earle, N., "Mode of Action of Pyrethrum and Pyrethrum Synergists", A Thesis, University of Illinois, 1954.
894. Early, J. D., and Cochran, J. H., The Journal of Economic Entomology 49(2): 239, 1956.
895. Easter, S. S., and Phillips, G. L., The Journal of Economic Entomology 36: 552, 1943.
896. Eaton, J. K., Compte Rendu; III^{e} Congrès international de phytopharmacie, Paris 1952, p. 346.
897. Eaton, J. K., Nature (London) 163: 496, 1949.
898. Eaton, J. K., Proceedings of the 2nd International Congress of Plant Protection, London 1949, p. 119.
899. Eaton, J. K., and Davies, R. G., Annals of Applied Biology 37: 92, 1950.
900. Ibid., 37: 471, 1950.
901. Eaton, J. K., and Davies, R. G., Nature (London) 161: 644, 1948.
902. Ebeling, W., The Journal of Economic Entomology 39: 795, 1946.
903. Ibid., 40: 619, 1947.
904. Ebeling, W., and Pence, R. J., Journal of Agricultural and Food Chemistry 1(5): 386, 1953.
905. Ebeling, W., and Pence, R. J., The Journal of Economic Entomology 47(5): 789, 1954.
906. Eckert, J. E., California Agricultural Experiment Station Circular No. 365, 1946.
907. Eckert, J. E., The Journal of Economic Entomology 37: 551, 1944.

908. Ibid., 38: 369, 1945.
909. Ibid., 41: 487, 1948.
910. Ibid., 42(2): 261, 1949.
911. Eckert, J. E., and Allinger, H. W., The Journal of Economic Entomology 28: 590, 1935.
912. Eddy, E. O., and Meadows, C. M., The Journal of Economic Entomology 30: 430, 1937.
913. Eddy, G. W., in "Insects", The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
914. Eddy, G. W., The Journal of Economic Entomology 42: 265, 1949.
915. Ibid. 45(6): 1043, 1952.
916. Eddy, G. W., et al., Soap and Sanitary Chemicals 30(7): 121, 1954.
917. Eddy, G. W., and Bushland, R. C., The Journal of Economic Entomology 41: 369, 1948.
918. Eddy, G. W., and Carson, N. B., The Journal of Economic Entomology 39: 763, 1946.
919. Ibid., 41: 31, 1948.
920. Eddy, G. W., and Graham, C. H., The Journal of Economic Entomology 42: 265, 1949.
921. Eddy, G. W., and McGregor, W. S., The Journal of Economic Entomology 42(3): 547, 1949.
922. Eden, W. G., The Journal of Economic Entomology 44(6): 1013, 1951.
923. Edson, E., et al., Technical Report for Pest Control Limited, 1954.
924. Edwards, J. E., and Dalton, A. J., Journal of the National Cancer Institute (Washington, D.C.) 3: 19, 1942.
925. Ehrenstein, M., Die Naturwissenschaften (Berlin) 16: 987, 1928.
926. Eichholz, Geuter, Deutsche medizinal Zeitschrift, 1887, p. 749.
927. Eide, P. M., The Journal of Economic Entomology 40(1): 49, 1947.
928. Eide, P. M., et al., The Journal of Economic Entomology 38: 492, 1945.
929. Ibid., 38(5): 537, 1945.
930. El Khishen, S. A., Compte Rendu; III^{e} Congrès international de phytopharmacie, Paris 1952, p. 469.
931. Eller, Dissertation, Wurzburg, 1939.
932. Elliott, E. W., Proceedings; Iowa Academy of Science 55: 99, 1948.
933. Elliott, J. M., Journal of the Royal Army Medical Corps (London) 60: 373, 1933.
934. Elliott, M., Pyrethrum Post 2(3): 18, 1951.
935. Elliott, M., et al., Annals of Applied Biology 37: 490, 1950.
936. Ellis, The Journal of Pharmacology and Experimental Therapeutics 91: 370, 1947.
937. Ellis, et al., The Journal of Pharmacology and Experimental Therapeutics 91: 255, 1947.
938. Ellis, M. M., American Wildlife 26: 38; 45, 1937.
939. Ellis, M. M., U.S. Department of Commerce, Bureau of Fisheries Bulletin No. 22, 1937.
940. Ellis, M. M., U.S. Department of Commerce, Bureau of Fisheries Special Scientific Report No. 1, p. 61, 1940.
941. Ellis, M. M., U.S. Department of the Interior Research Report No. 9, 1946.
942. Ellisor, L. O., Iowa State College Journal of Science 11: 51, 1936.
943. Ellisor, L. O., and Blair, C. R., The Journal of Economic Entomology 33(5): 760, 1940.
944. Ellisor, L. O., and Floyd, E. H., The Journal of Economic Entomology 31(1): 64, 1938.
945. Elmer, H. S., et al., The Journal of Economic Entomology 44(4): 593, 1951.
946. Ely, R. E., Journal of Dairy Science 36: 309, 1953.
947. Emery, G. A., Proceedings of the First International Congress of Plant Protection, Heverlee (The Netherlands) 1947, p. 351.
948. Enders, A., Archives internationales de pharmacodynamie et de thérapie (Paris) 89: 169, 1952.
949. Enders, A., and Grupp, G., Ärzneimittel-Forschung 1: 79, 1951.
950. Engbaek, L., and Jensen, O. S., Acta pharmacologica et toxicologica (København) 7: 189, 1951.
951. English, L. L., Outline, Illinois Custom Spray Operators' School, Urbana, Illinois, 1949.
952. English, L. L., The Journal of Economic Entomology 36(5): 737, 1943.
953. Ibid., 44(2): 208, 1951.
954. Ewing, K. P., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
955. Eyzaquirre, C., and Lilienthal, J. L., Proceedings of the Society for Experimental Biology and Medicine 70: 272, 1949.
956. Fabre, R., and Truhaut, R., British Journal of Industrial Medicine 8: 275, 1951.
957. Fahey, J. E., et al., The Journal of Economic Entomology 45: 700, 1952.
958. Fairchild, C. G., and Barreda, E. A., The Journal of Economic Entomology 38: 694, 1945.
959. Fairchild, H. E., et al., The Journal of Economic Entomology 42: 410, 1949.
960. Fairhall, L. T., Journal of the New England Water Works Association (Boston) 55: 400, 1941.
961. Fales, J. H., et al., The Journal of Economic Entomology 44(1): 23, 1951.
962. Ibid., 44(6): 991, 1951.
963. Ibid., 47(1): 27, 1954.
964. Ibid., 48(1): 49, 1955.
965. Fan, H., et al., Physiological Zoölogy 21: 48, 1948.
966. Farrar, M. D., Proceedings of the First International Congress of Plant Protection, Heverlee (The Netherlands) 1946, p. 416.
967. Fassig, W. W., and Campbell, F. L., The Journal of Economic Entomology 30: 681, 1937.
968. Faulkner, J. M., The Journal of the American Medical Association 100: 1664, 1933.
969. Faust, J. The Journal of the American Medical Association 141: 192, 1949.
970. Fay, R. W., The Journal of Economic Entomology 35(1): 45, 1942.
971. Fay, R. W., et al., The Journal of Economic Entomology 40: 635, 1947.
972. Fay, R. W., et al., The Journal of the National Malaria Society 8: 137, 1949.
973. Fay, R. W., et al., Public Health Reports (Washington, D.C.) (Supplement) 186: 21, 1945.
974. Fay, R. W., et al., Soap and Sanitary Chemicals 24(6): 130, 1948.
975. Feder, W. A., Bulletin of the New York State Flower Growers 82: 3, 1952.
976. Feils, G., Tierärztliche Umschau (Konstanz) 1954, part 11 / 12.
977. Feinstein, L., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
978. Feldberg, W., Physiological Review 25: 596, 1945.
979. Fellton, H. L., The Journal of Economic Entomology 33(2): 252, 1940.

980. Fenton, F. A., and Afanasiev, M., The Journal of Economic Entomology 39: 818, 1946.
981. Ferguson, G. R., and Alexander, C. C., Journal of Agricultural and Food Chemistry 1(14): 888, 1953.
982. Ferguson, G. R., and Ott, D. J., The Journal of Economic Entomology 46(6): 991, 1953.
983. Ferguson, J., Proceedings of the Royal Society (London) B127: 387, 1939.
984. Ferguson, J., and Pirie, H., Annals of Applied Biology 35: 532, 1948.
985. Ferguson, W., and Kearns, C., The Journal of Economic Entomology 42: 810, 1949.
986. Fernald, C. H., Massachusetts Agricultural Experiment Station Bulletin No. 24, 1894.
987. Fernando, B. B., et al., The Indian Journal of Medical Research (Calcutta) 26: 759, 1939.
988. Fernando, H., “Acetylcholine-like Material in Nervous Tissue of the American Roach”, Thesis, University of Illinois, 1953.
989. Fernando, H., et al., Annals of the Entomological Society of America 44: 551, 1951.
990. Fetscher, R., Reichs- Gesundheitsblatt (Berlin) 11: 228, 1927.
991. Ibid., 12: 253, 1927.
992. Fields, J., et al., Proceedings of the Society for Experimental Biology and Medicine 81: 678, 1952.
993. Fiesinger, N., et al., Bulletins et mémoires de la Société médicale des hôpitaux de Paris (Serie III) 46: 1210, 1922.
994. Fiesinger, N., and Wolf, M., Comptes rendus des séances de la Société de biologie (Paris) 87: 627, 1922.
995. Fife, L. C., et al., The Journal of Economic Entomology 41: 665, 1948.
996. Filmer, R. S., The Journal of Economic Entomology 30: 75, 1937.
997. Fink, D. E., Journal of Agricultural Research (Washington, D.C.) 33: 993, 1926.
998. Ibid., 45: 471, 1932.
999. Fink, D. E., The Journal of Economic Entomology 20: 794, 1927.
1000. Fink, D. E., et al., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine Circular E-425, 1938.
1001. Fink, D. E., and Vivian, D. L., The Journal of Economic Entomology 29(4): 804, 1936.
1002. Finnegan, J. K., et al., Archives internationales de pharmacodynamie et de thérapie (Paris) 103(4): 404, 1955.
1003. Finnegan, J. K., et al., Proceedings of the Society for Experimental Biology and Medicine 72: 357, 1949.
1004. Fischer, E., and Bernfeld, P., Helvetica chimica acta (Basel) 32: 1146, 1949.
1005. Fisher, E. H., and Allen, T. C., The Journal of Economic Entomology 38(3): 392, 1945.
1006. Fisher, H. J., and Baily, E. M., Connecticut Agricultural Experiment Station Bulletin No. 398, 1937.
1007. Fischer, R. A., Annals of the Entomological Society of America 29: 335, 1936.
1008. Fisher, R. A., Canadian Journal of Zoölogy 30: 254, 1952.
1009. Fisher, R. A., The Journal of Economic Entomology 33(5): 728, 1940.
1010. Fisher, R. A., and Shull, W. E., The Journal of Economic Entomology 35(4): 503, 1942.
1011. Fisk, F. W., The Journal of Economic Entomology 44(6): 1016, 1951.
1012. Fisk, F. W., and Isert, J. A., The Journal of Economic Entomology 46(6): 1059, 1953.
1013. Fisk, F. W., and Shepard, H. H., The Journal of Economic Entomology 31(1): 79, 1938.
1014. Fitzhugh, O. G., Reported by Cox, A. J. at U.S. Food and Drug Administration Hearings of Week Ending 9/12/1950.
1015. Fitzhugh, O. G., et al., Federation Proceedings 8: 291, 1949.
1016. Fitzhugh, O. G., et al., The Journal of Pharmacology and Experimental Therapeutics 100: 59, 1950.
1017. Fitzhugh, O. G., and Nelson, A. A., The Journal of Pharmacology and Experimental Therapeutics 89: 18, 1947.
1018. Flanders, S. E., The Journal of Economic Entomology 36: 469, 1943.
1019. Fleck, E., Journal of the American Chemical Society 71: 1034, 1949.
1020. Fleck, E., and Haller, H., Journal of the American Chemical Society 68: 142, 1946.
1021. Fleming, J. D., Water Pollution Abstracts 20: 1947.
1022. Fleming, W. E., The Journal of Economic Entomology 40: 932, 1947.
1023. Ibid., 41: 905, 1948.
1024. Fleming, W. E., New Jersey Agricultural Experiment Station Bulletin No. 410, 1925.
1025. Fleming, W. E., U.S. Department of Agriculture Technical Bulletin No. 788, 1942.
1026. Fleming, W. E., and Baker, F. E., Journal of Agricultural Research (Washington, D.C.) 52(7): 493, 1936.
1027. Ibid., 53: 187, 1936.
1028. Fleming, W. E., and Baker, F. E., U.S. Department of Agriculture Technical Bulletin No. 427, 1934.
1029. Fleming, W. E., and Maines, W. W., The Journal of Economic Entomology 40: 845, 1947.
1030. Fletcher, J., et al., Journal of the American Chemical Society 70: 3943, 1948.
1031. Ibid., 72: 2461, 1950.
1032. Flint, W. P., and Badulf, W. V., Illinois Agricultural Experiment Station Bulletin No. 249, 1924.
1033. Floyd, E. H., The Journal of Economic Entomology 40: 422, 1947.
1034. Floyd, E. H., and Smith, C. E., The Journal of Economic Entomology 42: 908, 1949.
1035. Flury, F., Abderhalden, Handbuch der biologischen Arbeitsmethoden 4.7b: p. 1307.
1036. Ibid., 4.7b: p. 1315.
1037. Ibid., 4.7b: p. 1340.
1038. Ibid., 4.7b: p. 1349.
1039. Ibid., 4.7b: p. 1374.
1040. Ibid., 4.7b: p. 1396.
1041. Ibid., 4.7b: p. 1406.
1042. Flury, F., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 138: 75, 1928.
1043. Flury, F., Archiv für Gewerbe pathologie und Gewerbehygiene (Berlin) 5: 1, 1934.
1044. Ibid., 5: 16, 1934.
1045. Flury F., and Zernik, F., “Schadliche Gase”, Julius Springer Verlag, Berlin, 1931.
1046. Fogg, G. E., Annals of Applied Biology 35: 315, 1948.
1047. Foot, E. B., et al., Anesthesiology 4: 283, 1943.
1048. Forbes, G., The British Medical Journal 1: 348, 1943.
1049. Forrest, J., et al., Journal of the Chemical Society 1946, p. 333.

1050. Forschungsdienst, in Angewandte Chemie 54: 499, 1941. (Water Pollution Abstracts 14: October, 1941).

1051. Forssling, S., Acta pharmacologica et toxicologica (København) 4: 143, 1948.

1052. Fox, C. J., and Perron, P., Entomological Society of Ontario (Canada), 76th Annual Report, 1945.

1053. Francone, M. P., et al., Revista de la Asociación médica argentina Buenos Aires) 66: 56, 1952.

1054. Frank, Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 64: 274, 1911.

1055. Franke, K. W., Proceedings of the Society for Experimental Biology and Medicine 29: 1177, 1932.

1056. Franke, K. W., and Moxon, A. L., The Journal of Pharmacology and Experimental Therapeutics 58: 454, 1936.

1057. Frawley, J. P., et al., The Journal of Pharmacology and Experimental Therapeutics 105: 156, 1952.

1058. Frawley, J. P., and Fitzhugh, O. G., Federation Proceedings 8: 292, 1949.

1059. Frear, D. E. H., "Chemistry of Insecticides, Fungicides, and Herbicides", Van Nostrand, New York, 1948.

1060. Frear, D. E. H., The Journal of Economic Entomology 37(5): 629, 1944.

1061. Frear, D. E. H., "Pesticide Handbook", 7th Edition, 1955, College Science Publishers, State College, Pennsylvania.

1062. Frear, D. E. H., et al., Maine Agricultural Experiment Station Miscellaneous Publication No. 613, 1949.

1063. Frederick, H. J., Utah Agricultural Experiment Station Bulletin No. 223, 1930.

1064. Fried, J., et al., Journal of the American Chemical Society 72: 4621, 1950.

1065. Ibid., 73: 2970, 1951.

1066. Friedman, N. H., United States Naval Medical Bulletin 41: 1792, 1943.

1067. Frings, H., and O'Tousa, J. E., Science 111: 658, 1950.

1068. Frois, M., Bulletin de l' Académie de médicine (Paris) 88: 40, 1922.

1069. Frost, D. V., and Richards, R. K., The Journal of Laboratory and Clinical Medicine 30: 138, 1945.

1070. Führer, H., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 97: 86, 1923.

1071. Führer, H., Biochemische Zeitschrift (Berlin) 120: 143, 1921.

1072. Fukuto, T. R., et al., The Journal of Economic Entomology 48(4): 347, 1955.

1073. Ibid., 49(2): 147, 1956.

1074. Fukuto, T. R., and Metcalf, R. L., Journal of the American Chemical Society 76: 5103, 1954.

1075. Fuller, G., Proceedings of the First International Congress of Plant Protection, Heverlee (The Netherlands) 1946, p. 411.

1076. Fuller, H. S., Annual Review of Entomology 1: 347, 1956.

1077. Fuller, R., et al., The Journal of Biological Chemistry 186: 823, 1950.

1078. Fullmer, O. H., and Hoskins, W. M., The Journal of Economic Entomology 44: 858, 1951.

1079. Fulmek, L., Archiv für Chemie und Mikroskopie in ihrer Anwendung auf den öffentlichen Verwaltungsdienst (etc.) (Wien) 6: 1, 1913.

1080. Fulton, B. B., The Journal of Economic Entomology 39: 781, 1946.

1081. Fulton, R. A., and Howard, N. F., The Journal Economic Entomology 31: 405, 1938.

1082. Fulton, R. A., and Mason, H. C., Journal of Agricultural Research (Washington, D.C.) 55: 903, 1937.

1083. Furman, D. P., The Journal of Economic Entomology 40: 518, 1947.

1084. Ibid., 40: 673, 1947.

1085. Furman, D. P., et al., California Agriculture 9(1): 13, 1955.

1086. Furman, D. P., and Douglass, J. R., The Journal of Economic Entomology 41: 781, 1948.

1087. Furman, D. P., and Kurtpinar, H., The Journal of Economic Entomology 43: 343, 1950.

1088. Furman, D. P., and Weinmann, C. J., The Journal of Economic Entomology 49(4): 447, 1956.

1089. Gage, J. C., Biochemical Journal (London) 54: 426, 1953.

1090. Gage, J. C., II^{e} Congrès international de biochemie, résumés des communications 1952, p. 433.

1091. Gahan, J. B., et al., The American Journal of Hygiene 49: 285, 1949.

1092. Gahan, J. B., et al., Journal of Agricultural and Food Chemistry 2(8): 425, 1954.

1093. Gahan, J. B., et al., The Journal of Economic Entomology 35(5): 669, 1942.

1094. Ibid., 41(5): 795, 1948.

1095. Ibid., 46(6): 965, 1953.

1096. Gaines, J. C., et al., The Journal of Economic Entomology 41: 510, 1948.

1097. Ibid., 43(5): 614, 1950.

1098. Ibid., 45(5): 790, 1952.

1099. Gaines, J. C., and Dean, H. A., The Journal of Economic Entomology 41: 808, 1948.

1100. Ibid., 41: 945, 1948.

1101. Ibid., 42(3): 429, 1949.

1102. Gaines, J. C., and Hanna, R. L., The Journal of Economic Entomology 44(1): 116, 1951.

1103. Gaines, R. C., The Journal of Economic Entomology 31(6): 659, 1938.

1104. Gallay, R., Compte Rendu; Premier Congrès international de phytopharmacie, Heverlee (Pays-Bas) 1947, p. 601.

1105. Galley, R. A. E., Report of the 5th Commonwealth Entomological Conference, Commonwealth Institute of Entomology, 1948.

1106. Gambrell, F. L., The Journal of Economic Entomology 33: 264, 1940.

1107. Ibid., 41: 770, 1948.

1108. Gardiner, J. E., and Kilby, B. A., Biochemical Journal (London) 46: xxxii, 1950.

1109. Ibid., 51: 78, 1952.

1110. Gardiner, J. E., and Kilby, B. A., Journal of the Chemical Society, 1950, p. 1769.

1111. Gardner, K., and Heath, D. F., Analytical Chemistry 25: 1849, 1953.

1112. Gardocki, J. F., and Hazelton, L. W., Journal of the American Pharmaceutical Association, Scientific Edition 40: 491, 1951.

1113. Garin, C., and Roman, E., Annales d'hygiène publique, industrielle et sociale (Paris), 1939, p. 56.

1114. Garlick, W. L., Industrial Hygiene Newsletter (Washington, D.C.) 10(9): 11, 1950.

1115. Garman, P., Connecticut Agricultural Experiment Station Bulletin No. 349, 1933, p. 433.

1116. Garman, P., The Journal of Economic Entomology 43(1): 53, 1950.

1117. Garrett, R. M., Journal of the Medical Association of Alabama (U. S.) 17: 74, 1947.
1118. Garrison, H. F., Southern Medical Journal (U.S.) 27: 24, 1934.
1119. Gasser, R., Transactions of the 9th International Congress of Entomology, Amsterdam, 1951, Volume II, p. 1037.
1120. Gasser, R., Berichte der Schweizerische botanische Gesellschaft 62: 66, 1952.
1121. Gasser, R., Compte Rendu; III^{e} Congrès international de phytopharmacie, Paris 1952, p. 357.
1122. Gasser, R., Experientia 8: 65, 1952.
1123. Gasser, R., Zeitschrift für Naturforschung (Weisbaden) 8b: 225, 1953.
1124. Gast, R. T., et al., The Journal of Economic Entomology 49(3): 408, 1956.
1125. Gates, D. B., The Journal of Economic Entomology 38(3): 391, 1945.
1126. Gates, F. H., Colorado Bureau of Plant Industry, Insect Control Report S-1-49, 1949.
1127. Gaudin, O., "Recherches sur l'Action physiologique des Pyrethrins", Vigot, Paris, 1937.
1128. Gause, G. F., and Smaragdova, N. P., Physiological Zoölogy 12: 238, 1939.
1129. Gay, F. J., Australia (Dominion of), Council of Scientific and Industrial Research Bulletin No. 225, 1947.
1130. Geary, J. T., Journal of Agricultural and Food Chemistry 1(14): 880, 1953.
1131. Geiger, W. B., and Conn, J. E., Journal of the American Chemical Society 67: 112, 1945.
1132. Geigy, J. R., Swiss Patent No. 279,553 (1952).
1133. Geigy, J. R., Swiss Patent No. 282,655 (1952).
1134. Geigy, J. R., (Société Anonyme) Technical Bulletins, 1953.
1135. Gekemans, J., Transactions of the 9th International Congress of Entomology, Amsterdam, 1951, p. 1052.
1136. Gelfand, M., Water Power Plant Engineering 45: 5; 60, 1941.
1137. Gellatly, J. G. G., Agricultural Gazette of New South Wales (Australia, Dominion of) 59: 540, 1948.
1138. Geoffroy, E., Annales de l'Institut colonial, Marseilles 2: 1, 1895.
1139. Geoffroy, E., Journal de pharmacie et de chimie (Paris) 26: 454, 1892.
1140. Gerber, E., Archiv der Pharmazie und Berichte der Deutschen pharmazeutischen Gesellschaft (Berlin) 241: 270, 1903.
1141. Gersdorff, W. A., Journal of Agricultural Research (Washington, D.C.) 50: 893, 1935.
1142. Gersdorff, W. A., Journal of the American Chemical Society 52: 3440, 1930.
1143. Ibid., 52: 5051, 1930.
1144. Ibid., 53: 1895, 1931.
1145. Ibid., 55: 2941, 1933.
1146. Ibid., 56: 979, 1934.
1147. Gersdorff, W. A., The Journal of Economic Entomology 40: 878, 1947.
1148. Ibid., 42: 532, 1949.
1149. Gersdorff, W. A., U. S. Department of Agriculture Miscellaneous Publication No. 117, 1932.
1150. Gersdorff, W. A., et al., The Journal of Economic Entomology 45(6): 905, 1952.
1151. Ibid., 47(5): 839, 1954.
1152. Gersdorff, W. A., et al., Soap and Sanitary Chemicals 26(4): 137, 1950.
1153. Gersdorff, W. A., and Clayborn, H., Journal of Agricultural Research (Washington, D.C.) 56: 277, 1938.
1154. Gersdorff, W. A., and Gertler, S. I., Soap and Sanitary Chemicals 20: 123, 1944.
1155. Gersdorff, W. A., and McGouran, E. R., The Journal of Economic Entomology 37(1): 137, 1944.
1156. Gersdorff, W. A., and McGouran, E. R., Soap and Sanitary Chemicals 21(11): 117, 121, 1945.
1157. Gersdorff, W. A., and Mitlin, N., The Journal of Economic Entomology 43(4): 554, 1950.
1158. Ibid., 43(4): 562, 1950.
1159. Ibid., 44(1): 70, 1951.
1160. Ibid., 45: 519, 1952.
1161. Ibid., 45(5): 849, 1952.
1162. Ibid., 46(6): 945, 1953.
1163. Ibid., 46(6): 999, 1953.
1164. Gersdorff, W. A., and Nelson, R. H., The Journal of Economic Entomology 41(2): 333, 1948.
1165. Gersdorff, W. A., and Piquett, P. G., The Journal of Economic Entomology 48(4): 407, 1955.
1166. Gertler, S. I., et al., Soap and Sanitary Chemicals 19(4): 105, 1945.
1167. Gettler, O., and Weiss, L., The American Journal of Clinical Pathology 13: 422, 1943.
1168. Giang, P. A., U. S. Department of Agriculture, Agricultural Research Service. Entomology Research Branch E-874, March 1954. "Bibliography of Systemic Insecticides".
1169. Giang, P. A., and Hall, S. A., Analytical Chemistry 23: 1830, 1951.
1170. Gilbert, E., and Giolito, S., U. S. Patents 2,616,825 and 2,616,928 (1952).
1171. Gilbert, I. H., et al., The Journal of Economic Entomology 46(1): 48, 1953.
1172. Gilbert, I. H., et al., U. S. Department of Agriculture Bulletin No. E-795, 1950.
1173. Gildmeister, Zeitschrift für die gesamte experimentelle Medizin (Berlin) 13: 291, 1921.
1174. Gile, P. L., Journal of Agricultural Research (Washington, D.C.) 52(7): 477, 1936.
1175. Gimingham, C., et al., Annals of Applied Biology 13: 446, 1926.
1176. Ginsburg, J. M., Agricultural Chemicals 3(5): 23, 1948.
1177. Ginsburg, J. M., 48th Annual Report of the New Jersey Agricultural Experiment Station, 1927.
1178. Ginsburg, J. M., Journal of Agricultural and Food Chemistry 3(4): 322, 1955.
1179. Ginsburg, J. M., Journal of Agricultural Research (Washington, D.C.) 43: 469, 1931.
1180. Ibid., 46: 1131, 1933.
1181. Ginsburg, J. M., The Journal of Economic Entomology 25: 918, 1932.
1182. Ibid., 28: 292, 1935.
1183. Ibid., 30: 583, 1937.
1184. Ibid., 38(2): 274, 1945.
1185. Ibid., 41: 649, 1948.
1186. Ibid., 42: 602, 1949.
1187. Ginsburg, J. M., Science 105: 233, 1947.
1188. Ginsburg, J. M., et al., Journal of Agricultural Research 51: 349, 1935.
1189. Ginsburg, J. M., et al., The Journal of Economic Entomology 28: 236, 1935.
1190. Ginsburg, J. M., and Cavallito, G. J., The Journal of Economic Entomology 29(5): 856, 1936.
1191. Ginsburg, J. M., and Mann, R. F., The Journal of Economic Entomology 42: 646, 1949.
1192. Gjullin, C. M., et al., The Journal of Economic Entomology 42(1): 100, 1949.

1193. Gjullin, C. M., et al., Mosquito News 13(1): 4, 1953.

1194. Glaser, E., and Frisch, S., Archiv für Hygiene und Bakteriologie (München) 101: 48, 1929.

1195. Glasgow, H., Farm Research (New York State Agricultural Experiment Station, Geneva, New York) 2: 3; 7; 13, 1936.

1196. Glasgow, H., The Journal of Economic Entomology 22: 335, 1929.

1197. Glass, E. H., The Journal of Economic Entomology 37(1): 74, 1944.

1198. Ibid., 43(1): 146, 1950.

1199. Glass, E. H., and Chapman, P. J., The Journal of Economic Entomology 42(1): 29, 1949.

1200. Glass, E. H., and Crozier, W. F., The Journal of Economic Entomology 42: 646, 1949.

1201. Glass, E. H., and Fiori, B., The Journal of Economic Entomology 48(5): 598, 1955.

1202. Glendenning, R., Department of Agriculture, Canada; Division of Entomology Proceedings No. 48, 1948.

1203. Ibid., No. 52, 1946.

1204. Glover, L., and Richardson, C., Iowa State College Journal of Science 10: 249, 1936.

1205. Gnadinger, C., "Pyrethrum Flowers", McLaughlin, Gormley, King Co., Minneapolis 1936.

1206. Ibid., Supplement, 2nd Edition 1936 - 1945.

1207. Gnadinger, C., and Corl, C., Journal of the American Chemical Society 51: 3054, 1929.

1208. Ibid., 52: 3300, 1930.

1209. Goble, C. J., and Patton, R. L., The Journal of Economic Entomology 39(2): 177, 1936.

1210. Godfrey, G. H., and Young, P. A., Texas Agricultural Experiment Station Bulletin No. 628, 1943.

1211. Gokhale, V. C., and Bhide, B. V., Journal of the Indian Chemical Society 22: 250, 1945.

1212. Gold, H., and Brown, F., The Journal of Pharmacology and Experimental Therapeutics 54: 463, 1935.

1213. Goldblatt, M. U., The Pharmaceutical Journal (London) 164: 229, 1950.

1214. Goldstein, F., and Rieders, F., The American Journal of Physiology 173: 287, 1953.

1215. Goldsworthy M., and Green, E., Phytopathology 29: 700, 1939.

1216. Golz, H. H., and Shaffer, C. B., "Malathion, Summary of Pharmacology and Toxicity", (Revised January 1955) Central Medical Department, American Cyanamid Company.

1217. Gooden, E. L., Industrial and Engineering Chemistry 33: 1452, 1941.

1218. Goodhue, L. D., et al., The Journal of Economic Entomology 35: 553, 1942.

1219. Goodhue, L. D., and Sullivan, W. N., The Journal of Economic Entomology 34(1): 77, 1941.

1220. Goodman, L., and Gilman, A., "The Pharmacological Basis of Therapeutics", McMillan, New York, 1941.

1221. Ibid., Second Edition, 1955.

1222. Goodnight, C. J., Industrial and Engineering Chemistry 34: 868, 1942.

1223. Goodrum, P., et al., Journal of Wildlife Management 13: 1, 1949.

1224. Goodson, J. A., Biochemical Journal (London) 15: 123, 1921.

1225. Goodwin-Bailey, K. F., and Davies, M., Nature (London) 173: 216, 1954.

1226. Gordon, H., and Welsh, J., The Journal of Cellular and Comparative Physiology 31: 395, 1948.

1227. Gosswald, K., Zeitschrift für angewandte Entomologie (Berlin) 20: 489, 1934.

1228. Ibid., 21: 1, 1934.

1229. Goudey, R. F., Journal of the American Water Works Association 38: 186, 1946.

1230. Goudey, R. F., Western Construction News 11: 295, 1936.

1231. Gough, H. C., Annals of Applied Biology 26: 533, 1939.

1232. Ibid., 27: 101, 1940.

1233. Gould, G. E., Indiana Agricultural Experiment Station Bulletin No. 490, 1944.

1234. Gould, G. E., Soap and Sanitary Chemicals 24(3): 147, 1948.

1235. Gould, E., and Hampstead, E. O., The Journal of Economic Entomology 41: 887, 1948.

1236. Gove, J. F., and Bovingdon, H. H. S., Annals of Applied Biology 34: 113, 1947.

1237. Gowdey, C. A., et al., Canadian Journal of Medical Sciences 30: 520, 1952.

1238. Ibid., 32: 498, 1954.

1239. Graeve, K., and Herrnring, G., Archives internationales de pharmacodynamie et de thérapie (Paris) 85: 64, 1951.

1240. Graeve, K., and Herrnring, G., Klinische Wochenschrift (Berlin) 28: 622, 1950.

1241. Graham, C., The Journal of Economic Entomology 42: 354, 1949.

1242. Graham, C., and Cory, E. N., The Journal of Economic Entomology 39: 816, 1946.

1243. Graham, K., Transactions of the Royal Society of Canada 40: (Section 5) 41, 1946.

1244. Graham, S. A., Annual Review of Entomology 1: 261, 1956.

1245. Grandjean, L. C., Ugeskrift for laeger (København) 112: 86, 1950.

1246. Granett, P., et al., The Journal of Economic Entomology 42(2): 281, 1949.

1247. Ibid., 44(1): 97, 1951.

1248. Ibid., 44(4): 552, 1951.

1249. Granett, P., and French, C. F., The Journal of Economic Entomology 43(1): 41, 1950.

1250. Ibid., 44(1): 93, 1951.

1251. Granett, P., and Haynes, H. L., The Journal of Economic Entomology 38: 671, 1945.

1252. Granett, P., and Shea, W. D., The Journal of Economic Entomology 48(4): 487, 1955.

1253. Granger, M., and Leiby, R. W., Agricultural Chemicals 4(2): 34, 1949.

1254. Granovsky, A. A., The Journal of Economic Entomology 19: 791, 1926.

1255. Ibid., 37: 493, 1944.

1256. Gray, G. P., and De Ong, E. R., Industrial and Engineering Chemistry 18: 175, 1926.

1257. Gray, K. W., and Schuh, J., The Journal of Economic Entomology 33: 72, 1940.

1258. Grayson, J. M., The Journal of Economic Entomology 46: 888, 1953.

1259. Ibid., 47(2): 253, 1954.

1260. Grayson, J. M., et al., The Journal of Economic Entomology 49(1): 130, 1956.

1261. Grayson, J. M., and King, E. W., The Journal of Economic Entomology 36(4): 540, 1943.

1262. Grayson, J. M., and Poos, F. W., The Journal of Economic Entomology 40: 251, 1947.

1263. Grayson, J. M., and Swank, G. R., The Journal of Economic Entomology 34(1): 65, 1941.

1264. Greaves, T., Journal of the Council for Scientific and Industrial Research (Australia) 18: 110, 1945.
1265. Green, D. E., et al., The Journal of Biological Chemistry 172: 389, 1948.
1266. Greenbank, J., Transactions. The American Fisheries Society 70: 80, 1940.
1267. Greenslade, R. M., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, p. 307.
1268. Greenwood, D., Physiological Review 20: 582, 1940.
1269. Greenwood, D., The Journal of Economic Entomology 40: 724, 1947.
1270. Greenwood, M., The Journal of Physiology (London) 11: 573, 1890.
1271. Gregson, J. D., The Canadian Entomologist 78: 201, 1946.
1272. Griffiths, J. T., et al., The Journal of Economic Entomology 44(1): 160, 1951.
1273. Griffiths, J. T., and Tauber, O. E., The Journal of Economic Entomology 36(4): 536, 1943.
1274. Grigsby, B. H., et al., Michigan Agricultural Experiment Station Circular No. 214, 1949.
1275. Grimm, V., et al., Vierteljahrsschrift für gerichtliche Medizin und öffnentliches sanitätswessen Dritte Folge p. 161, 1914, (Supplement).
1276. Grindley, J., Annals of Applied Biology 33: 103, 1946.
1277. Grob, D., Annals of Internal Medicine 32: 1229, 1950.
1278. Grob, D., Bulletin of the Johns Hopkins Hospital 87: 95, 1950.
1279. Grob, D., et al., Annals of Internal Medicine 31: 899, 1949.
1280. Grob, D., et al., Bulletin of the Johns Hopkins Hospital 81: 217, 1947.
1281. Ibid., 87: 106, 1950.
1282. Grob, D., et al., The Journal of the American Medical Association 153: 529, 1953.
1283. Grob, D., and Harvey, A. M., The American Journal of Medicine 12: 52, 1953.
1284. Grob, D., and Harvey, A. M., Bulletin of the Johns Hopkins Hospital 84: 532, 1949.
1285. Grob, H., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris, 1952, p. 389.
1286. Grob, H., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, Volume II, p. 1042.
1287. Grummit, O., Science 111: 361, 1950.
1288. Grummit, O., et al., Journal of the American Chemical Society 67: 155; 2265, 1945.
1289. Gubler, H. W., et al., Schweizerische Bienen-Zeitung (Bern) 7: 268, 1953.
1290. Guilhon, M. J., Comptes rendus hebdomadaires des séances de l'Académie d'Agriculture de France, (Ministère d'Agriculture) 32: 158, 1946.
1291. Gulland, J. M., and Hopton, G. U., Journal of the Chemical Society, 1930, p. 62.
1292. Gunderson, H., and Strand, A. L., The Journal of Economic Entomology 32(1): 106, 1939.
1293. Gunn, D. L., et al., Anti-Locust Research Centre, Department of Agriculture of South Africa (Union of), 1947.
1294. Gunn, W. C., Department of Health for Scotland (Great Britain) Report No. 2, 1933.
1295. Günthart, E., Mitteilungen. Schweizerische entomologische Gesellschaft, 1947.
1296. Günthart, E., and Clausen, R. L., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952, p. 403.
1297. Gunther, F. A., Journal of the American Chemical Society 67: 189, 1945.
1298. Gunther, F. A., and Blinn, R. C., Annual Review of Entomology 1: 167, 1956.
1299. Gunther, F. A., and Blinn, R. C., Journal of the American Chemical Society 69: 1215, 1947.
1300. Ibid., 72: 5770, 1950.
1301. Gunther, F. A., et al., Analytical Chemistry 23: 1835, 1951.
1302. Gunther, F. A., et al., The Journal of Economic Entomology 48(4): 372, 1955.
1303. Gurney, R., Gastroenterology (Baltimore) 12: 1112, 1943.
1304. Gustafson, C., et al., The Journal of Economic Entomology 46: 620, 1953.
1305. Guthrie, F. E., et al., The Journal of Economic Entomology 43(4): 559, 1950.
1306. Ibid., 47(2): 215, 1954.
1307. Guthrie, F. E., et al., The Journal of Economic Entomology 49(5): 602, 1956.
1308. Guthrie, F. E., and Baker, F. S., Florida Entomologist 37: 13, 1954.
1309. Gutsell, J. S., Bureau of Fisheries Document 910, Appendix to Report of the U.S. Commission of Fisheries, 1921.
1310. Guy, H., Delaware Agricultural Experiment Station Bulletin No. 206, 1937.
1311. Guyton, T. L., Pennsylvania State Department of Agriculture General Bulletin No. 473.
1312. Gyrisko, G. G., et al., The Journal of Economic Entomology 42: 311, 1949.
1313. Gyrisko, G. G., and Marshall, D. S., The Journal of Economic Entomology 43(1): 82, 1950.
1314. Ibid., 43: 438, 1950.
1315. Gysin, H., Belgian Patent 510,817 (1952).
1316. Gysin, H., Chimia (Zürich) 8: 205, 1954.
1317. Gysin, H., Compte Rendu, III^{me} Congrès international de phytopharmacie, Paris 1952, p. 412.
1318. Haag, H. B., The Journal of Pharmacology and Experimental Therapeutics 43: 113, 1937.
1319. Ibid., 48: 95, 1943.
1320. Haag, H. B., Proceedings of the Society for Experimental Biology and Medicine 54: 140, 1943.
1321. Haag, H. B., Soap and Sanitary Chemicals 13(1): 112, 1937.
1322. Haag, H. B., et al., Archives internationales de pharmacodynamie et de thérapie (Paris) 83: 491, 1950.
1323. Haag, H. B., et al., Industrial Medicine 17: 477, 1948.
1324. Haas, H., Archiv für experimentelle Pathologie und Pharmakologie 189: 397, 1938.
1325. Haas, H., et al., Industrial and Engineering Chemistry 43: 2875, 1951.
1326. Hadjinicolau, J., and Hansens, E. J., The Journal of Economic Entomology 46(1): 34, 1953.
1327. Hadley, C. H., and Fleming, W. E., in "Insects" The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
1328. Haenseler, C. M., and Martin, W. H., Phytopathology 15: 321, 1935.
1329. Häfliger, E., Experientia 4: 223, 1948.
1330. Häfliger, E., The Journal of Economic Entomology 42(3): 523, 1949.
1331. Hagan, E. C., Federation Proceedings 12: 327, 1952.

1332. Hagan, E. C., and Woodard, J. E., Federation Proceedings 6: 335, 1947.
1333. Ibid., 7: 224, 1948.
1334. Hagen, J., and Reinl, W., Münchener medizinische Wochenschrift 92: 449, 1950.
1335. Hagen, W., The Progressive Fish-Culturist 48: 19, 1940.
1336. Haines, K. A., The Journal of Economic Entomology 41: 513, 1948.
1337. Hall, M. C., and Schillinger, J. E., The American Journal of Tropical Medicine 5: 229, 1925.
1338. Hall, M. C., and Schillinger, J. E., The North American Veterinarian 9: 41, 1925.
1339. Hall, S. A., Advances in Chemistry Series 1: 150, 1950.
1340. Hall, S. A., Analytical Chemistry 23: 1866, 1951.
1341. Hall, S. A., and Jacobson, M., Industrial and Engineering Chemistry 40: 694, 1948.
1342. Hall, W. E. B., Annals of Western Medicine and Surgery 5: 1025, 1951.
1343. Haller, H. L., Agricultural Chemicals 2(9): 26, 1947.
1344. Haller, H. L., Industrial and Engineering Chemistry (Industrial Edition) 39: 467, 1947.
1345. Haller, H. L., et al., Journal of the American Chemical Society 67: 1591, 1945.
1346. Haller, H. L., et al., The Journal of Economic Entomology 35(2): 247, 1942.
1347. Haller, H. L., et al., The Journal of Organic Chemistry 7: 183, 1942.
1348. Ibid., 7: 185, 1942.
1349. Haller, H. L., and Bowen, C. V., Agricultural Chemicals 2(1): 15, 1947.
1350. Haller, H. L., and La Forge, F. B., The Journal of Organic Chemistry 2: 49, 1937.
1351. Hallock, H. C., and Deen, O. T., The Journal of Economic Entomology 49(1): 123, 1956.
1352. Hamblin, D. O., Agricultural Chemicals 1(6): 28, 1946.
1353. Hamblin, D. O., and Marchand, J. F., American Practitioner and Digest of Treatment 2: 1, 1951.
1354. Hamblin, D. O., and Marchand, J. F., Annals of Internal Medicine 36: 50, 1952.
1355. Hamersma, P. J., Union of South Africa Department of Agriculture and Forestry Scientific Bulletin No. 236, 1943.
1356. Hamilton, A., and Johnstone, R. T., "Industrial Toxicology" in "Oxford Medicine" IV, part 2, Oxford University Press, 1944.
1357. Hamilton, C. C., The Journal of Economic Entomology 40(5): 733, 1947.
1358. Hamilton, D. A., et al., The Journal of Economic Entomology 47(5): 768, 1954.
1359. Hamilton, D. W., The Journal of Economic Entomology 40(2): 234, 1947.
1360. Ibid., 43: 694, 1950.
1361. Ibid., 49(6): 866, 1956.
1362. Hamilton, D. W., Proceedings of the New York State Horticultural Society 91: 200, 1946.
1363. Hamilton, D. W., and Fahey, J. E., The Journal of Economic Entomology 47(2): 361, 1954.
1364. Hamilton, H. L., The Journal of Cellular and Comparative Physiology 13: 91, 1939.
1365. Hamlin, J. C., and Reed, W. D., The Journal of Economic Entomology 20: 400, 1927.
1366. Hamman, R. E., Data Contributed by, on Behalf of the Shell Chemical Corporation, Agricultural Chemicals Division, 1956.
1367. Hamman, R. E., The Journal of Economic Entomology 41(3): 516, 1948.
1368. Hamman, R. E., quoting Archives of Industrial Hygiene and Occupational Medicine 7: 118, 1953.
1369. Hammer, O. H., American Fruit-Grower 68: 22, 1948.
1370. Hammer, O. H., The Journal of Economic Entomology 42: 380, 1949.
1371. Hammer, R. E., The Journal of Economic Entomology 41: 516, 1948.
1372. Hammet, F. S., and Nowrey, J. E., The Journal of Pharmacology and Experimental Therapeutics 19: 331, 1922.
1373. Handford, R. H., Department of Agriculture (Canada) Division of Entomology Proceedings, Publication No. 86, 1948.
1374. Hanna, A. D., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952, p. 426.
1375. Hanna, A. D., et al., Nature (London) 169: 334, 1952.
1376. Hansberry, R., The Journal of Economic Entomology 33(5): 734, 1940.
1377. Ibid., 35: 915, 1942.
1378. Hansberry, R., et al., The Journal of Economic Entomology 33(3): 511, 1940.
1379. Hansberry, R., and Lee, C., The Journal of Economic Entomology 36: 351, 1943.
1380. Hansberry, R., and Norton, L., The Journal of Economic Entomology 34(1): 80, 1941.
1381. Hansberry, R., and Richardson, C. H., The Journal of Economic Entomology 29(6): 1160, 1936.
1382. Hansen, J. W., The Journal of Economic Entomology 40: 600, 1947.
1383. Hansens, E. J., The Journal of Economic Entomology 46(2): 246, 1953.
1384. Ibid., 46(2): 372, 1953.
1385. Ibid., 49(1): 27, 1956.
1386. Hansens, E. J., and Bartley, G., The Journal of Economic Entomology 46(2): 372, 1953.
1387. Hansens, E. J., and Scott, R., The Journal of Economic Entomology 48(3): 337, 1955.
1388. Hanzel, R. F., et al., Federation Proceedings 13: 363, 1953.
1389. Hard, M. M., and Ross, E., Journal of Agricultural and Food Chemistry 2(1): 20, 1954.
1390. Harding, W. C., The Journal of Economic Entomology 48(5): 605, 1955.
1391. Harding, W. C., and Quigley, G. D., The Journal of Economic Entomology 49(6): 806, 1956.
1392. Hare, K. P., and Dutta, S. C., The Indian Medical Gazette (Calcutta) 74: 198, 1939.
1393. Hargreaves, E., Bulletin of Entomological Research (London) 15: 521, 1924.
1394. Haring, R. C., The Journal of Economic Entomology 39(1): 78, 1946.
1395. Harman, R. E., The Journal of Economic Entomology 41: 516, 1948.
1396. Harper, S., Annual Reports on the Progress of Chemistry (Chemical Society, London) 45: 162, 1948.
1397. Harper, S., et al., Annals of Applied Biology, 34: 104, 1947.
1398. Harper, S., et al., Chemistry and Industry, 1949 p. 636.
1399. Harper, S., et al., Journal of the Science of Food and Agriculture 2: 94, 1951.
1400. Harrar, N. J., Scientific Monthly 25: 246, 1927.
1401. Harries, F. H., The Journal of Economic Entomology 37(1): 151, 1944.

1402. Harries, F. H., et al., Journal of Agricultural Research (Washington, D.C.) 71: 553, 1945.
1403. Harries, F. H., and Matsumori, H., The Journal of Economic Entomology 49(1): 131, 1956.
1404. Harries, F. H., and Valcarce, A. C., The Journal of Economic Entomology 48(5): 614, 1955.
1405. Harris, C. S., Proceedings of the American Society of Horticultural Science 60: 335, 1952.
1406. Harris, J. R., et al., Archives of Biochemistry 21: 370, 1949.
1407. Harris, J. S., Agricultural Chemicals 2(10): 27, 1947.
1408. Harris, L. E., Journal of the American Pharmaceutical Association 37: 145, 1948.
1409. Harris, W., et al., U.S. Patent No. 2,529,494 (1950).
1410. Harris, W. D., and Zukel, J. W., Journal of Agricultural and Food Chemistry 2(3): 140, 1954.
1411. Harrison, C., The Journal of Economic Entomology 46: 528, 1953.
1412. Harrison, C., Transactions of the Royal Society of Tropical Medicine and Hygiene (London) 46: 255, 1952.
1413. Hart, E. R., and Conn, L. W., The Journal of Pharmacology and Experimental Therapeutics 98: 12, 1950.
1414. Hartley, G. S., Chemistry and Industry, 1951, p. 123.
1415. Hartley, G. S., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952, p. 131.
1416. Hartley, G. S., Transactions of the 15th International Chemical Congress, New York 1951.
1417. Hartley, G. S., et al., Journal of the Science of Food and Agriculture 2(7): 303, 1951.
1418. Hartley, G. S., and Heath, D. F., Nature (London) 167: 816, 1951.
1419. Hartley, G. S., and Kilby, B., Nature, (London) 166: 784, 1950.
1420. Hartzell, A., Contributions from the Boyce Thompson Institute 6: 211, 1934.
1421. Ibid., 13: 243, 1944.
1422. Ibid., 13: 443, 1945.
1423. Ibid., 15: 337, 1949.
1424. Hartzell, A., The Journal of Economic Entomology 22: 354, 1929.
1425. Hartzell, A., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, Volume I, p. 1047.
1426. Hartzell, A., and Scudder, H., The Journal of Economic Entomology 35: 428, 1942.
1427. Hartzell, A., and Storrs, E. E., Contributions from the Boyce Thompson Institute 16(2): 47, 1950.
1428. Hartzell, A., and Wexler, E., Contributions from the Boyce Thompson Institute 14(3): 123, 1946.
1429. Hartzell, A., and Wilcoxon, F., Contributions from the Boyce Thompson Institute 4: 107, 1932.
1430. Ibid., 6: 269, 1934.
1431. Ibid., 8: 183, 1936.
1432. Ibid., 12: 1, 1941.
1433. Hartzell, A., and Wilcoxon, F., The Journal of Economic Entomology 23: 608, 1930.
1434. Hartzell, F. Z., et al., The Journal of Economic Entomology 28: 263, 1935.
1435. Hartzell, F. Z., and Moore, J. B., The Journal of Economic Entomology 30: 651, 1937.
1436. Hartzell, F. Z., and Parrott, P. J., New York State Agricultural Experiment Station Bulletin No. 636, 1933.
1437. Harukawa, C., Transactions. The American Fisheries Society 52: 219, 1922.
1438. Harvey, A. M., Proceedings of the Institute of Medicine of Chicago 17: 182, 1948.
1439. Harvey, D. G., et al., British Medical Journal, 2: 13, 1951.
1440. Harvey, G. E. R., and Swenson, K. G., The Journal of Economic Entomology 47(4): 564, 1954.
1441. Harvey, G. T., and Brown, A. W. A., Canadian Journal of Zoölogy 29: 42, 1951.
1442. Harvey, T. L., The Journal of Economic Entomology 47(4): 593, 1954.
1443. Harvill, E., Contributions from the Boyce Thompson Institute 10: 143, 1939.
1444. Harvill, E., et al., Contributions from the Boyce Thompson Institute 13: 87, 1943.
1445. Harwood, et al., The Journal of Parasitology 24: 16, 1938.
1446. Hase, A., Zeitschrift für wissenschaftliche Biologie, Abteilung F, Zeitschrift für Parasitenkunde (Berlin) 4: 369, 1932.
1447. Hastings, E., and Pepper, E. H., The Journal of Economic Entomology 42: 554, 1949.
1448. Hatcher, The American Journal of Physiology 11: 17, 1904.
1449. Hatfield, I., Pests, 17: 9, 1949.
1450. Haug, G. W., and Peterson, A., The Journal of Economic Entomology 31(1): 87, 1938.
1451. Haviland, E., and Highland, H., The Journal of Economic Entomology 48(3): 326, 1955.
1452. Haworth, R., et al., Journal of the Chemical Society, 1947, p. 176.
1453. Hayes, W. J., and Liu, Y. - S., Annals of the Entomological Society of America 40: 401, 1947.
1454. Hayes, W. J., et al., The American Journal of Tropical Medicine 31(4): 519, 1951.
1455. Haymaker, W., et al., The American Journal of the Medical Sciences 212: 423, 1946.
1456. Haynes, H., et al., Contributions from the Boyce Thompson Institute 18: 1, 1954.
1457. Hazelhoff, E. H., The Journal of Economic Entomology 21: 790, 1928.
1458. Hazleton, L. W., Journal of Agricultural and Food Chemistry 3(4): 312, 1955.
1459. Ibid., 3(10): 836, 1955.
1460. Hazleton, L. W., and Godfrey, E., Federation Proceedings 7: 226, 1948.
1461. Hazleton, L. W., and Holland, E. G., Archives of Industrial Hygiene and Occupational Medicine 8: 399, 1953.
1462. Hazleton, L. W., and Holland, E. G., Advances in Chemistry Series 1: 31, 1950.
1463. Headden, W. P., Colorado Agricultural Experiment Station Bulletin No. 131, p. 157.
1464. Heal, R. E., Agricultural Chemicals 4(5): 37, 1949.
1465. Heal, R. E., et al., The Journal of Economic Entomology 46(2): 385, 1953.
1466. Heal, R. E., et al., Lloydia 13: 89, 1950.
1467. Heap, R., and Saunders, B., Journal of the Chemical Society, 1948, p. 1313.
1468. Heath, D. F., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952.
1469. Heath, D. F., et al., Journal of the Science of Food and Agriculture 3: 60, 1952.
1470. Ibid., 3: 69, 1952.

1471. Heath, D. F., et al., Transactions of the Royal Society (London) Series B 239(663): 191, 1955.
1472. Heath, D. F., and Casapieri, P., Transactions, The Faraday Society 47: 1093, 1951.
1473. Hecht, G., Deutsche medizinische Wochenschrift (Leipzig) 77: 783, 1952.
1474. Hecht, G., Institute for Industrial Hygiene and Toxicology, Farbenfabriken Bayer, Wuppertal-Elberfeld (Germany).
1475. Hecht, G., and Wirth, W., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 211: 264, 1950.
1476. Hedenburg, O. F., and Wachs, H., Journal of the American Chemical Society 70: 2216, 1948.
1477. Heffter, Heffter's Handbuch der experimentelle Pharmakologie 3.1: p. 79.
1478. Heimann, H., New York State Industrial Bulletin 23: 103, 1944.
1479. Hely, P. C., Agricultural Gazette of New South Wales (Australia) 58: 85, 1947.
1480. Ibid., 59: 144, 1948.
1481. Henderson, C. F., The Journal of Pharmacology and Experimental Therapeutics 57: 394, 1936.
1482. Henderson, C. F., and Tilton, E. W., The Journal of Economic Entomology 48(2): 157, 1955.
1483. Hennig, A., et al., Journal of the American Pharmaceutical Association, Scientific Edition 40: 168, 1951.
1484. Henry, T., "The Plant Alkaloids", J. and A. Churchill, London, 1939.
1485. Hensill, G. S., Agricultural Chemicals 4(9): 29, 1949.
1486. Heppel, L. A., et al., Archives of Opthalmology (Chicago) 32: 391, 1944.
1487. Heppel, L. A., et al., The Journal of Industrial Hygiene and Toxicology 26: 8, 1944.
1488. Ibid., 28: 1, 1946.
1489. Ibid., 28: 113, 1946.
1490. Ibid., 30: 189, 1948.
1491. Heppel, L. A., et al., The Journal of Pharmacology and Experimental Therapeutics 84: 53, 1945.
1492. Ibid., 87: 11, 1946.
1493. Ibid., 91: 385, 1947.
1494. Heppel, L. A., and Neal, P. A., The Journal of Industrial Hygiene and Toxicology 26: 17, 1944.
1495. Hepple, R. A., Journal of the Royal Army Medical Corps (London) 49: 442, 1927.
1496. Hercules Powder Company, Advertisement in Journal of Economic Entomology, 1950.
1497. Hercules Powder Company, Bulletin No. 461.
1498. Herdt, J. R., et al., Public Health Reports (Washington, D.C.) 66: 1313, 1951.
1499. Herken, H., et al., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 215: 217, 1952.
1500. Herken, H., and Klempau, I., Die Naturwissenschaften 37: 493, 1950.
1501. Herrick, G. W., "Insect Enemies of Shade Trees", Comstock, Ithaca, New York, 1935.
1502. Herrick, G. W., and Griswold, G. H., The Journal of Economic Entomology 25: 243, 1932.
1503. Ibid., 26: 446, 1933.
1504. Herzfeld, S., and Ordas, E., British Patent 652,300 (1951).
1505. Hetrick, J., The Journal of Economic Entomology 43(1): 57, 1950.
1506. Heubner, W., and Papierkowski, J., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 188: 605, 1938.
1507. Heukelekian, H., Sewage and Industrial Wastes 25: 633, 1953.
1508. Hewlett, P. S., Bulletin of Entomological Research (London) 43: 21, 1952.
1509. Hewlett, P. S., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952, p. 438.
1510. Hewlett, P. S., Nature (London) 173: 132, 1954.
1511. Hey, G. L., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952, p. 433.
1512. Hey, G. L., Grower 26: 14, 1946.
1513. Ibid., May 7, 1952, p. 29.
1514. Heymans, C., Archives internationales de pharmacodynamie et de thérapie (Paris) 50: 20, 1935.
1515. Heymans, C., et al., Archives internationales de pharmacodynamie et de thérapie (Paris) 77: 486, 1948.
1516. Ibid., 79: 123, 1949.
1517. Heymans, C., and Estable, J., Sciences (Paris) 109: 22, 1949.
1518. Heymans, C., and de Vleeschower, G., Archives internationales de pharmacodynamie et de thérapie (Paris) 75: 307, 1948.
1519. Heyroth, F. F., "DDT", (a Monograph [in mimeograph]) February, 1950.
1520. Heyroth, F. F., Public Health Reports (Washington, D.C.) Supplement 197, p. 1, 1947.
1521. Hicks, C., and Sinclair, D., Australian Journal of Experimental Biology and Medical Science (Adelaide) 25: 83, 1947.
1522. Hicks, D. W., Texas State Journal of Medicine 50: 148, 1954.
1523. Hieringa, J. W., and Swarbrick, T., Annals of Applied Biology 39: 213, 1952.
1524. Higgons, D. J., and Kilbey, D. W., Chemistry and Industry, 1954 (October), p. 1359.
1525. Highman, B., et al., Archives of Pathology (Chicago) 51: 346, 1951.
1526. Highman, B., and Heppel, L. A., Archives of Pathology (Chicago) 42: 525, 1946.
1527. Hill, J. L., Journal of the Council for Scientific and Industrial Research (Australia [Melbourne]) 19: 251, 1946.
1528. Hill, K. R., and Robinson, G., British Medical Journal 2: 845, 1945.
1529. Hill, R. E., Nebraska Agricultural Experiment Station Bulletin No. 138, 1945.
1530. Hill, R. E., et al., The Journal of Economic Entomology 41: 392, 1948.
1531. Hill, R. E., and Hixon, E., The Journal of Economic Entomology 40: 137, 1947.
1532. Hill, W. R., and Damiani, C. R., New England Journal of Medicine 235: 897, 1946.
1533. Hinds, W. E., The Journal of Economic Entomology 2: 161, 1909.
1534. Ibid., 4: 532, 1911.
1535. Hinman, E. J., The Journal of Economic Entomology 37(1): 148, 1944.
1536. Hinman, F. G., The Journal of Economic Entomology 47(4): 540, 1954.
1537. Ibid., 47(4): 549, 1954.
1538. Hirsch, A. A., Botanical Gazette 103: 620, 1942.
1539. Hirschmann, H., Höfchen-Briefe für Wissenschaft und Praxis (Bayer Pflanzenschutz Nachrichten) 6: 90, 1953.
1540. Hirz, Zeitschrift für Biologie (München) 60: 187, 1913.
1541. Hitchcock, L., Australian Journal of Agricultural Research 4: 360, 1953.

1542. Hitchener, L.S., in "Insects", The Yearbook of Agriculture 1952. U.S. Department of Agriculture (Washington, D.C.).

1543. Hobbiger, F., British Journal of Pharmacology and Chemotherapy 9: 159, 1954.

1544. Hobson, R. P., Annals of Applied Biology 28: 273, 1941.

1545. Hockenyos, G. L., The Journal of Economic Entomology 29: 433, 1936.

1546. Ibid., 32: 843, 1939.

1547. Hockenyos, G. L., Soap and Sanitary Chemicals 21(3): 109, 1945.

1548. Hockenyos, G. L., and Lilly, J., The Journal of Economic Entomology 25: 253, 1932.

1549. Hocking, B., Scientific Agriculture 30: 489, 1950.

1550. Hocking, K. S., Reports; Colonial Institute of Research Laboratory, Entebbe, Uganda Proctectorate, 1948.

1551. Hodge, H. C., et al., The Journal of Pharmacology and Experimental Therapeutics 99(1): 140, 1950.

1552. Ibid., 104(1): 60, 1952.

1553. Ibid., 112(1): 29, 1954.

1554. Hoegberg, E. I., and Cassaday, J. T., Journal of the American Chemical Society 73: 557, 1951.

1555. Hoerner, J. L., and Edmundson, W. C., The Journal of Economic Entomology 40: 603, 1947.

1556. Höfbauer, Dissertation, Würzburg, 1933.

1557. Hofferbert, W., and Orth, H., Höfchen-Briefe für Wissenschaft und Praxis (Bayer Pflanzenschutz Nachrichten) 5: 10, 1052.

1558. Hoffman, J. R., The Journal of Economic Entomology 41(3): 356, 1948.

1559. Hoffman, R. A., et al., The Journal of Economic Entomology 42: 893, 1949.

1560. Ibid., 47(1): 72, 1954.

1561. Hoffman, R. A., and Lindquist, A. W., The Journal of Economic Entomology 42: 891, 1949.

1562. Ibid., 45: 233, 1952.

1563. Hoffmann, Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 205: 223, 1948.

1564. Hoffmann, C. H., and Merkel, E. P., The Journal of Economic Entomology 41(3): 464, 1948.

1565. Hoffmann, C. H., and Surber, E. W., The Progressive Fish- Culturist, 1949 (October), p. 203.

1566. Hoffmann, C. H., and Surber, E. W., Transactions. The American Fisheries Society 75: 48, 1945.

1567. Hoffmann, C. H., and Surber, E. W., U.S. Department of the Interior. Fish and Wildlife Service Special Scientific Report No. 3, 1949.

1568. Hofmann, E. C., Nachrichten über Schädlingsbekämpfung der I. G. Farbenindustrie Aktiengesellschaft (Leverkusen b. Köln am Rhein) 14: 1, 1938.

1569. Hofmann, E. C., Zeitschrift für angewandte Entomologie (Berlin) 25: 381, 1938.

1570. Hofmann-Credner, D., and Siedek, H., Archives internationales de pharmacodynamie et de thérapie 89: 74, 1952.

1571. Hofmaster, R. N., and Anderson, L. D., The Journal of Economic Entomology 41(1): 198, 1948.

1572. Hofmaster, R. N., and Greenwood, D. E., The Journal of Economic Entomology 42(4): 502, 1949.

1573. Holdaway, F. G., et al., Proceedings of the Hawaiian Entomological Society 12: 301, 1945.

1574. Holdaway, F. G., et al., Report of the Agricultural Experiment Station, University of Hawaii, 1948.

1575. Holland, E. B., and Read, J. C., Report of the Massachusetts Agricultural Experiment Station, 1912.

1576. Holland, J. M., Data contributed on Behalf of the Rohm and Haas Company, January 1956.

1577. Holland, J. M., Federation Proceedings 11: 357, 1952.

1578. Holloway, J. K., et al., The Journal of Economic Entomology 35: 348, 1942.

1579. Holloway, T. E., et al., U.S. Department of Agriculture Circular No. 45, 1928.

1580. Holman, H., "Insecticide Materials of Vegetable Origin", Imperial Institute, London 1940.

1581. Holmstedt, B., Acta physiologica Scandinavica (Stockholm) 25: supplement 90, 1951.

1582. Hoobler, S., Dontas, A., Physiological Review 5: 135, 1953.

1583. Hopf, H. S., Annals of Applied Biology 39: 193, 1952.

1584. Ibid., 41: 248, 1954.

1585. Hopf, H. S., Proceedings of the Second International Congress of Crop Protection, London 1949, p. 213.

1586. Hopperstead, S. L., Agricultural Chemicals 2: 24, 1947.

1587. Horn, H. J., et al., Journal of Agricultural and Food Chemistry 3(9): 752, 1955.

1588. Hornstein, I., et al., The Journal of Economic Entomology 48(4): 482, 1955.

1589. Horton, R. G., et al., Science 107: 246, 1948.

1590. Hoskins, J. K., Industrial and Engineering Chemistry, News Edition 19: 1138, 1941.

1591. Hoskins, W. M., Compte Rendu; III^{me} Congres international de phytopharmacie, Paris 1952, p. 443.

1592. Hoskins, W. M., Hilgardia 13: 307, 1940.

1593. Hoskins, W. M., The Journal of Economic Entomology 25: 1212, 1932.

1594. Ibid., 34: 791, 1941.

1595. Hoskins, W. M., et al., The Journal of Economic Entomology 33: 875, 1940.

1596. Hoskins, W. M., and Craig, R., Annual Review of Biochemistry 25: 539, 1946.

1597. Hoskins, W. M., and Gordon, H. T., Annual Review of Entomology 1: 89, 1956.

1598. Hotai, N., Journal of the College of Agriculture of the Imperial University of Tokyo (Japan) 25: 69, 1941.

1599. Hotchkiss, N., and Pough, R. H., Journal of Wildlife Management 10: 202, 1946.

1600. Hottinger, and Bloch, Helvetica chimica acta (Basel) 26: 142, 1943.

1601. Hough, W. S., Journal of Agricultural Research (Washington, D.C.) 38: 248, 1929.

1602. Ibid., 48: 533, 1934.

1603. Hough, W. S., The Journal of Economic Entomology 21: 325, 1928.

1604. Ibid., 27: 1102, 1934.

1605. Ibid., 41(2): 207, 1948.

1606. Ibid., 41: 983, 1948.

1607. Hough, W. S., Virginia Agricultural Experiment Station Technical Bulletin No. 91, 1943.

1608. Hough, W. S., Virginia Fruit 33: 183, 1945.

1609. Howard, H., U.S. Patent No. 1,475,155.

1610. Howard, J. W., et al., Federation Proceedings 13: 339, 1954.

1611. Howard, J. W., and Hanzol, R. F., Journal of Agricultural and Food Chemistry 3(4): 325, 1955.

1612. Howard, N. F., The Journal of Economic Entomology 36(1): 59, 1943.
1613. Howard, N. F., et al., U.S. Department of Agriculture Miscellaneous Publication No. 526, 1943.
1614. Howe, W. L., The Journal of Economic Entomology 43: 549, 1950.
1615. Howe, W. L., and Miller, L. I., The Journal of Economic Entomology 47(4): 74, 1954.
1616. Hoyle, G., The Journal of Experimental Biology (London) 30: 121, 1953.
1617. Hrenoff, A. K., and Leake, C. D., University of California Publications in Pharmacology 1: 151, 1939.
1618. Hsing, Yun Fan, The Journal of Economic Entomology 40(6): 883, 1947.
1619. Huckett, H. C., The Journal of Economic Entomology 41(1): 202, 1948.
1620. Huisman, H. O., et al., Nature (London) September 10, 1955.
1621. Hunt, Archives internationales de pharmacodynamie et de thérapie (Paris) 12: 447, 1904.
1622. Hunt, W. T., The Journal of Economic Entomology 37(1): 136, 1944.
1623. Hurd-Karrer, A. M., Journal of Agricultural Research (Washington, D.C.) 54: 601, 1937.
1624. Hurd-Karrer, A. M., Smithsonian Institution of Washington (D.C.) Annual Report 1934-1935, p. 289.
1625. Hurd-Karrer, A. M., and Poos, F. W., Science 84: 252, 1936.
1626. Hurst, H., Nature (London) 145: 462, 1940.
1627. Ibid., 156: 194, 1945.
1628. Ibid., 163: 286, 1949.
1629. Hurst, H., Transactions; The Faraday Society 39: 390, 1943.
1630. Hurt, R. H., Virginia Agricultural Experiment Station Bulletin No. 293, 1933.
1631. Hutchinson, Widdowson, Nature (London) 169: 284, 1952.
1632. Hutzel, J. M., The Journal of Economic Entomology 35: 929, 1942.
1633. Hwang, L., and Klotz, L. J., Hilgardia 12: 1, 1938.
1634. Hyman, Julius, British Patent No. 618,432 (1949).
1635. Hyman (Julius) and Company, Newsletter, February 1950.
1636. Hyman (Julius) and Company, Newsletter, November 1950, quoting Radeleff, R. D.
1637. Hyman (Julius) and Company (Denver, Colorado) Technical Supplement No. 202, 1948.
1638. Hymas, F. C., Food Research 9: 254, 1940.
1639. Hyre, R. A., Cornell University (Ithaca, N.Y.) Agricultural Experiment Station Memoir No. 222, 1939.
1640. Iglinsky, W., and Gaines, J. C., The Journal of Economic Entomology 42(4): 703, 1949.
1641. Ikaw, M., et al., The Journal of Biological Chemistry 159: 517, 1945.
1642. Iljinskaya, M. I., Comptes rendus; Académie des sciences de l' U.R.S.S. (Moskva) 51: 557, 1946.
1643. Incho, H. H., and Ault, A. K., The Journal of Economic Entomology 47(4): 669, 1954.
1644. Incho, H. H., and Greenberg, H., The Journal of Economic Entomology 45(5): 794, 1952.
1645. Ingle, L., The Journal of Economic Entomology 40: 264, 1947.
1646. Ingle, L., Science 118: 213, 1953.
1647. Ingle, L., Technical Bulletin. Velsicol Corporation, Chicago.
1648. Ingram, F. R., American Industrial Hygiene Association Quarterly 12: 165, 1951.
1649. Ingram, J. W., et al., The Journal of Economic Entomology 40: 770, 1947.
1650. Ibid., 41: 914, 1948.
1651. Inoue, Y., et al., Botyu Kagaku (Kyoto) 16: 153, 1951.
1652. Irish, D. D., et al., The Journal of Industrial Hygiene and Toxicology 22: 218, 1940.
1653. Ibid., 23: 408, 1941.
1654. Isaac, W. E., Review of Applied Entomology (London) A 34: 189, 1946.
1655. Isely, D., Arkansas Agricultural Experiment Station Bulletin No. 462, 1948.
1656. Ivy, E. E., Agricultural Chemicals 8(4): 47, 1953.
1657. Ivy, E. E., The Journal of Economic Entomology 43: 590, 1950.
1658. Ivy, E. E., et al., The Journal of Economic Entomology 43: 620, 1950.
1659. Ibid., 46(4): 630, 1953.
1660. Ibid., 47(6): 1148, 1954.
1661. Ivy, E. E., and Ewing, K. P., The Journal of Economic Entomology 39(1): 38, 1946.
1662. Jacks, H., The New Zealand Journal of Science and Technology (Wellington) 28: 166, 1947.
1663. Jackson, A. C., and Lefroy, H. M., Bulletin of Entomological Research (London) 7: 327, 1917.
1664. Jackson, K., Chemical Reviews (Baltimore) 29: 123, 1941.
1665. Jacobs, M. B., "Analytical Chemistry of Industrial Poisons, Hazards and Solvents", Interscience, New York, 1941.
1666, Jacobs, T., et al., The Journal of Organic Chemistry (Baltimore) 16: 1572, 1951.
1667. Jacobson, M., Journal of the American Chemical Society 70: 4234, 1948.
1668. Ibid., 71: 366, 1949.
1669. Ibid., 72: 1480, 1950.
1670. Ibid., 73: 100, 1951.
1671. Jacobson, M., et al., Industrial and Engineering Chemistry 16: 166, 1944.
1672. Jacobson, M., et al., The Journal of Organic Chemistry (Baltimore) 12: 731, 1947.
1673. James, H. C., Proceedings of the 1946 Meeting of British West Indies Sugar Technologists.
1674. Jameson, H. R., et al., Annals of Applied Biology 34: 346, 1947.
1675. Ibid., 38: 121, 1951.
1676. Jancke, O., Anzeiger für Schädlingskunde (Berlin) 9: 55; 68, 1934.
1677. Jandorf, B. J., et al., Journal of the American Chemical Society 74: 1521, 1952.
1678. Jandorf, B. J., et al., The Journal of Pharmacology and Experimental Therapeutics 88: 333, 1946.
1679. Jandorf, B. J., and McNamara, B. P., The Journal of Pharmacology and Experimental Therapeutics 98: 77, 1950.
1680. Janisch, R., Nachrichtenblatt für den deutschen Pflanzenschutzdienst 6(3): 18, 1926.
1681. Jansen, E., et al., The Journal of Biological Chemistry 175: 975, 1948.
1682. Ibid., 179: 189, 1949.
1683. Ibid., 179: 201, 1949.
1684. Ibid., 190: 557, 1951.
1685. Jansen, E., and Balls, A., The Journal of Biological Chemistry 194: 721, 1952.
1686. Jantzen, G., Deutsche medizinische Wochenschrift (Leipzig) 76: 1601, 1951.
1687. Jary, S. G., Compte Rendu III^{me} Congrès international de phytopharmacie, Paris 1952, p. 452.

1688. Jaynes, H. A., and Marucci, P. E., The Journal of Economic Entomology 40(1): 9, 1947.
1689. Jefferson, R. N., The Journal of Economic Entomology 36(2): 253, 1943.
1690. Ibid., 46(1): 120, 1953.
1691. Jefferson, R. N., and Pence, R. J., The Journal of Economic Entomology 41(5): 653, 1948.
1692. Jelinek, A., U.S. Patent No. 2,503,390 (1950).
1693. Jensen, J. A., et al., Archives of Industrial Hygiene and Occupational Medicine 6: 326, 1952.
1694. Jensen, J. A., and Pearce, G., Journal of the American Chemical Society 74: 3184, 1952.
1695. Jeppson, L. R., Journal of Agricultural and Food Chemistry 1(13): 830, 1953.
1696. Jeppson, L. R., The Journal of Economic Entomology 39: 813, 1946.
1697. Ibid., 44(3): 328, 1951.
1698. Ibid., 44(6): 823, 1951.
1699. Ibid., 45(2): 271, 1952.
1700. Ibid., 45(4): 669, 1952.
1701. Jeppson, L. R., et al., The Journal of Economic Entomology 48(4): 375, 1955.
1702. Joachimoglu, G., Klinische Wochenschrift (Berlin) 58: 147, 1921.
1703. Joachimoglu, G., Biochemische Zeitschrift (Berlin) 70: 144, 1915.
1704. Johansen, C., The Journal of Economic Entomology 47(4): 715, 1954.
1705. Ibid., 49(5): 645, 1956.
1706. Johansen, C., et al., The Journal of Economic Entomology 47(5): 746, 1954.
1707. Johnson, A. C., et al., The Journal of Economic Entomology 35(5): 674, 1942.
1708. Johnson, F. H., et al., "Kinetic Basis of Molecular Biology", Wiley, 1954.
1709. Johnson, G. A., et al., The Journal of Economic Entomology 45(2): 279, 1952.
1710. Johnson, G. M., The Journal of the Florida Medical Association (Jacksonville) 36: 417, 1950.
1711. Johnson, M. O., and Godfrey, C. H., Industrial and Engineering Chemistry 24: 311, 1932.
1712. Johnson, W. T., et al., The Journal of Economic Entomology 49(1): 77, 1956.
1713. Johnston, B. L., and Eden, W. G., The Journal of Economic Entomology 46(4): 702, 1953.
1714. Joint Committee on Damage to Fisheries, "Road Tars and Fish Life", Surveyor (London) 78: 625, 1930.
1715. Jonas, H., Zeitschrift für Naturforschung (Wiesbaden) 7b: 132, 1952.
1716. Jones, E. P., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952, p. 491.
1717. Jones, G., and Edwards R., Bulletin of Entomological Research (London) 43: 67, 1952.
1718. Jones, G. D. G., and Connell, J. U., Annals of Applied Biology 41: 271, 1954.
1719. Jones, G. D. G., and Thomas, W. D. E., Annals of Applied Biology 40: 546, 1953.
1720. Jones, H., Journal of the American Chemical Society 53: 2738, 1931.
1721. Jones, H., et al., Soap and Sanitary Chemicals 21(11): 110, 1945.
1722. Jones, H., U.S. Department of Agriculture Bureau of Entomology and Plant Quarantine E-571, 1942.
1723. Jones, H. A., et al., The Journal of Economic Entomology 26: 451, 1933.
1724. Ibid., 39(5): 672, 1946.
1725. Jones, Jr., H. W., et al., The Journal of Pharmacology and Experimental Therapeutics 94: 215, 1948.
1726. Jones, H., and Smith, C., Journal of the American Chemical Society 52: 2554, 1930.
1727. Jones, J. R. E., The Journal of Experimental Biology (London) 18: 170, 1941.
1728. Jones, M. A., et al., The Journal of Economic Entomology 39(3): 281, 1946.
1729. Jones, R. M., Industrial and Engineering Chemistry 25: 394, 1933.
1730. Jones, R. M., The Journal of Economic Entomology 26: 895, 1933.
1731. Ibid., 28: 475, 1935.
1732. Ibid., 31(2): 298, 1938.
1733. Jones, S. C., The Journal of Economic Entomology 41(1): 118, 1948.
1734. Jones, S. E., and Mecom, W. H., The Journal of Economic Entomology 28: 650, 1935.
1735. Judah, J. D., Biochemical Journal (London) 49: 271, 1951.
1736. Judah, J. D., British Journal of Pharmacology and Chemotherapy 4: 120, 1949.
1737. Judah, J. D., Proceedings of the Royal Society of Medicine (London) 45: 574, 1952.
1738. Judah, J. D., and Williams-Ashman, H. G., Proceedings of the Second International Congress of Crop Protection, London 1949, p. 237.
1739. Jude, A., and Girard, P., Annales de médecine légale (Paris) 29: 209, 1949.
1740. Jungfer, Zentralblatt für Gewerbehygiene und Unfallverhütung (Berlin) 2: 222, 1914.
1741. Kabat, H., et al., The Journal of Pharmacology and Experimental Therapeutics 80: 160, 1944.
1742. Kagy, J. F., The Journal of Economic Entomology 29(2): 397, 1936.
1743. Ibid., 34(5): 660, 1941.
1744. Kagy, J. F., and McCall, G. L., The Journal of Economic Entomology 34(1): 119, 1941.
1745. Kagy, J. F., and Richardson, C. H., The Journal of Economic Entomology 29(1): 52, 1936.
1746. Kamm, and Marvel, "Organic Synthesis", Volume I, p. 3, 1921.
1747. Kansas State Board of Pharmacy, Report.
1748. Karel, Federation Proceedings 6: 342, 1947.
1749. Karsten, A., Journal of the American Water Works Association 28: 660, 1936.
1750. Kassab, A., Ministry of Agriculture, Egypt, Bulletin No. 193, 1939.
1751. Kauer, K., et al., Industrial and Engineering Chemistry 39: 1335, 1947.
1752. Kay, K., Canadian Journal of Public Health 41: 374, 1950.
1753. Kay, K., et al., Archives of Industrial Hygiene and Occupational Medicine 6: 252, 1952.
1754. Kay, K., et al., "Parathion Exposure and Choline Esterase Response of Quebec Apple Growers" (mimeograph), 1951.
1755. Kearns, C. W., Annual Review of Entomology 1: 123, 1956.
1756. Kearns, C. W., et al., The Journal of Economic Entomology 38: 661, 1945.
1757. Ibid., 42(1): 127, 1949.
1758. Keener, G. G., and Hess, A. D., Journal of Wildlife Management 11: 1, 1947.
1759. Kehoe, R. A., et al., Journal of the American Water Works Association 36: 645, 1944.
1760. Kehoe, R. A., et al., Journal of Industrial Hygiene and Toxicology 21: 160, 1939.
1761. Keiding, J., Science 123 (3209): 1173, 1956.
1762. Keiding, J., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, Volume II, p. 340.

1763. Keller, J. C., The Journal of Economic Entomology 48(5): 528, 1955.
1764. Keller, J. C., et al., The Journal of Economic Entomology 49(6): 751, 1956.
1765. Keller, J. C., and Chapman, H. C., The Journal of Economic Entomology 46(6): 1004, 1953.
1766. Ibid., 47(4): 628, 1954.
1767. Kelley, W. P., Transactions and Proceedings; American Society of Civil Engineers 106: 849, 1941.
1768. Kelly, R. B., et al., Canadian Journal of Chemistry 29: 905, 1951.
1769. Kelsheimer, E. G., Down to Earth 4: 2, 1948.
1770. Kemp, H. K., Journal of the Department of Agriculture of South Australia 51: 184, 1947.
1771. Kenaga, E. E., The Journal of Economic Entomology 42(6): 998, 1949.
1772. Ibid., 43(6): 938, 1950.
1773. Ibid., 49(6): 723, 1956.
1774. Kenaga, E. E., and Hummer, R., The Journal of Economic Entomology 42(6): 996, 1949.
1775. Kendrick, J., The American Journal of Tropical Medicine 9: 483, 1929.
1776. Kennedy, J. S., et al., British Museum, London, Anti-Locust Bulletin No. 2, 1948.
1777. Kent, D. L., et al., Soap and Sanitary Chemicals 29(6): 157, 1953.
1778. Kerr, R., Australia, Commonwealth Scientific and Industrial Research Organization Bulletin No. 2, 1948.
1779. Ibid., Bulletin No. 261, 1951.
1780. Kerr, T. W., The Journal of Economic Entomology 41(1): 48, 1948.
1781. Ibid., 43(1): 63, 1950.
1782. Ibid., 44(4): 493, 1951.
1783. Ketelaar, J. A. A., Proceedings of the Second International Congress of Crop Protection, London 1949, p. 239.
1784. Ketelaar, J. A. A., Recueil des travaux chimiques des Pays-Bas (et de la Belgique) (Amsterdam) 69: 649, 1950.
1785. Ketelaar, J. A. A., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, Volume II, p. 318.
1786. Ketelaar, J. A. A., and Gersmann, H., Journal of the American Chemical Society 72: 5777, 1950.
1787. Ketelaar, J. A. A., and Hellingman, J. E., Analytical Chemistry 23: 646, 1951.
1788. Kido, G. S., The Journal of Economic Entomology 34: 766, 1941.
1789. Kiessling, W., Biochemische Zeitschrift (Berlin) 114: 292, 1921.
1790. Kilby, B., Chemistry and Industry, 1953, p. 856.
1791. Kilby, B., and Kilby, M., British Journal of Pharmacology and Chemotherapy 2: 234, 1947.
1792. Kilby, B., and Youatt, G., Biochimica et biophysica acta (Amsterdam) 8: 112, 1952.
1793. Kilgore, L. B., et al., Industrial and Engineering Chemistry 34: 494, 1942.
1794. Kilpatrick, J. W., and Schoof, H. F., The Journal of Economic Entomology 47(6): 999, 1954.
1795. Ibid., 48(5): 623, 1955.
1796. King, E., and Harvey, D. G., Biochemical Journal (London) 53: 185; 196, 1953.
1797. King, H. L., and Frear, D. E. H., The Journal of Economic Entomology 36: 263, 1943.
1798. Ibid., 37(5): 629, 1944.
1799. King, H. L., and Hulson, R., The Journal of Economic Entomology 42: 398, 1949.
1800. King, K. M., and Forbes, A. R., The Journal of Economic Entomology 47(4): 607, 1954.
1801. King, W. V., "Chemicals Evaluated as Insecticides and Repellents at Orlando, Florida", U. S. Department of Agriculture, Agricultural Research Service, Agriculture Handbook No. 69, 1954.
1802. King, W. V., in "Insects", The Yearbook of Agriculture 1952. U. S. Department of Agriculture, Washington, D.C.
1803. King, W. V., The Journal of Economic Entomology 43(4): 527, 1950.
1804. Ibid., 44(3): 338, 1951.
1805. King, W. V., and Gahan, J. B., The Journal of Economic Entomology 42: 405, 1949.
1806. Kingscote, A. A., et al., Entomological Society of Ontario (Canada) 82nd Annual Report, 1951, p. 37.
1807. Kirby, A. H. M., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952, p. 463.
1808. Ibid., p. 483.
1809. Kirby, A. H. M., Lancet 249: 722, 1945.
1810. Kirby, A. H. M., and McKinlay, K., Annual Report of the East Malling Agricultural and Horticultural Research Station (Kent, Great Britain) 1950, p. 164.
1811. Kirby, A. H. M., and Read, W. H., Journal of the Science of Food and Agriculture 5: 327, 1954.
1812. Kirby, A. H. M., and Tew, R. P., Reports on the Progress of Applied Chemistry, (Society of Chemical Industry, London) XXXVII 263, 1952.
1813. Kirchner, J. G., Iowa State College Journal of Science 14: 53, 1939.
1814. Kirchner, J. G., and Richardson, C. H., The Journal of Economic Entomology 35(4): 525, 1942.
1815. Kirkor, T., Sewage Works Journal 23: 938, 1951.
1816. Kirkwood, S., and Dacey, J., Canadian Journal of Research 24B: 69, 1946.
1817. Kirkwood, S., and Phillips, P., The Journal of Biological Chemistry 163: 251, 1946.
1818. Kirkwood, S., and Phillips, P., The Journal of Pharmacology and Experimental Therapeutics 87: 375, 1946.
1819. Kistler, G. H., and Luckhardt, A. B., Anesthésie et analgésie 8: 65, 1929.
1820. Kitchel, R. L., and Hoskins, W. M., The Journal of Economic Entomology 28: 924, 1935.
1821. Klingemann, H., Aerztliche Wochenschrift (Berlin) 4: 465, 1949.
1822. Klinger, H., Arbeiten über physiologische und angewandte entomologie aus Berlin-Dahlem (Berlin. Biologische Reichsanstalt für Land- und Forst-wirtschaft; Kaiser Wilhelm-gesellschaft. Deutsches entomologisches Institut) 3: 49, 115, 1936.
1823. Klosa, J., Die Pharmazie (Berlin) 5: 615, 1950.
1824. Klosa, J., Zeitschrift für Naturforschung (Wiesbaden) 6b: 49, 1951.
1825. Klostermeyer, E. C., et al., The Journal of Economic Entomology 49(2): 164, 1956.
1826. Knight, H., et al., Plant Physiology 4: 299, 1929.
1827. Knight, K. L., The Journal of Economic Entomology 33(3): 536, 1940.
1828. Knipling, E. F., in "Insects". The Yearbook of Agriculture 1952. U. S. Department of Agriculture, Washington, D.C.
1829. Knipling, E. F., The Journal of Economic Entomology 34: 314, 1941.
1830. Ibid., 35(1): 63, 1942.

1831. Knipling, E. F., Soap and Sanitary Chemicals 25: 107, 1949.

1832. Knipling, E. F., et al., The Journal of Parasitology 34: 55, 1948.

1833. Knipling, E. F., and Dove, W. E., The Journal of Economic Entomology 37: 477, 1944.

1834. Knowles, F. L., et al., Public Health Reports (Washington, D.C.) 56: 1637, 1941.

1835. Knox, W. E., The Journal of Biological Chemistry 176: 117, 1948.

1836. Kochmann, M., Münchener medizinische Wochenschrift 75: 1334, 1928.

1837. Kodama, J., Archives of Industrial Hygiene and Occupational Medicine 9: 45, 1954.

1838. Koehlsch, F., Münchener medizinische Wochenschrift 62: 1567, 1915.

1839. Koehlsch, F., Zentralblatt für Gewerbehygiene und Unfallverhütung (Berlin) Neue Folge 264, 1930.

1840. Koelle, G. B., The Journal of Pharmacology and Experimental Therapeutics 100: 158, 1950.

1841. Ibid., 103: 153, 1951.

1842. Koelle, G. B., et al., The Journal of Pharmacology and Experimental Therapeutics 100: 180, 1950.

1843. Koelle, G. B., and Gilman, A., The Journal of Pharmacology and Experimental Therapeutics 95: 166, 1949.

1844. Koelle, G. B., and Gilman, A., Pharmacological Reviews (Baltimore) 1: 166, 1949.

1845. Köhne, H., Dissertation, Hamburg 1940.

1846. Kok, G. C., and Walop, J. N., Biochimica et biophysica acta (Amsterdam) 13: 510, 1954.

1847. Kolb, R. W., et al., Archives of Industrial Hygiene and Occupational Medicine 5: 354, 1952.

1848. Kolbezen, M., et al., Journal of Agricultural and Food Chemistry 2(17): 864, 1954.

1849. Konecky, M. S., and Mitlin, N., The Journal of Economic Entomology 48(2): 219, 1955.

1850. Konst, H., and Plummer, P. J. G., Canadian Journal of Comparative Medicine 14: 90, 1950.

1851. Koppanyi, T., et al., Science 106: 492, 1947.

1852. Körting, A., Zeitschrift für Pflanzenkrankheiten (Pflanzenpathologie) und Pflanzenschutz (Stuttgart) 43: 502, 1933.

1853. Kostov, D., Nature (London) 162: 845, 1948.

1854. Kowal, R. J., Down to Earth 5(2): 12, 1949.

1855. Kowal, R. J., and St. George, R. A., The Journal of Economic Entomology 41: 112, 1948.

1856. Krahl, M. E., and Clowes, G. H. A., Proceedings of the Society for Experimental Biology and Medicine 32: 226, 1934.

1857. Krayer, O., et al., The Journal of Pharmacology and Experimental Therapeutics 82: 167, 1944.

1858. Krayer, O., and Acheson, G. H., Physiological Review 26: 383, 1946.

1859. Krieger, C. H., Agricultural Chemicals 1(4): 19, 1946.

1860. Krieger, C. H., Soap and Sanitary Chemicals 22(9): 135, 1946.

1861. Krijgsman, B. J., et al., Bulletin of Entomological Research (London) 41: 141, 1950.

1862. Krijgsman, B. J., and Krijgsman, N. E., Nature (London) 165: 936, 1950.

1863. Krister, C. J., Agricultural Chemicals 6(7): 39, 1951.

1864. Krogh, P. M. D., and Tooke, F. G. C., Publications of the Department of Agriculture and Forestry, South Africa (Union of), 1946.

1865. Krüger, F., Zeitschrift für angewandte Entomologie (Berlin) 18: 344, 1931.

1866. Krukoff, B. A., and Smith, A. C., American Journal of Botany 24: 573, 1937.

1867. Krusé, C. W., et al., The Journal of Economic Entomology 45(4): 598, 1952.

1868. Kuenen, D. J., Tijdschrift over Plantenziekten (Amsterdam. Phytopathologisch Laboratorium "Willie Commelin Scholten") 49: 130, 1943.

1869. Ibid., 52: 69, 1946.

1870. Kühn, H. A., Transactions of the IVth International Congress of Entomology 1929, p. 673.

1871. Kühn, W., and Massini, P., Helvetica chimica acta (Basel) 32: 1530, 1949.

1872. Kulash, W. M., The Journal of Economic Entomology 40: 640, 1947.

1873. Ibid., 40: 926, 1947.

1874. Ibid., 41: 387, 1948.

1875. Ibid., 42: 502, 1949.

1876. Ibid., 42: 558, 1949.

1877. Ibid., 43(4): 430, 1950.

1878. Kuna, S., and Heal, R. E., The Journal of Pharmacology and Experimental Therapeutics 93: 407, 1948.

1879. Kunze, F. M., et al., Federation Proceedings 8: 311, 1949.

1880. Ibid., 9: 293, 1950.

1881. Kunze, F. M., et al., Proceedings of the Society for Experimental Biology and Medicine 75: 415, 1950.

1882. Kwoczek, J., Medizinische Monatsschrift (Stuttgart) 4: 25, 1950.

1883. Laake, E. W., Agricultural Chemicals 4: 39, 1949.

1884. Laake, E. W., The Journal of Economic Entomology 42(1): 143, 1949.

1885. Lackey, J. B., and Steinle, M. L., Public Health Reports (Washington, D.C.) Supplement No. 186, 1945.

1886. Lackey, R. W., The Journal of Industrial Hygiene and Toxicology 31: 117, 1949.

1887. LaForge, F. B., Journal of the American Chemical Society 64: 187, 1942.

1888. LaForge, F. B., The Journal of Organic Chemistry (Baltimore) 12: 199, 1947.

1889 LaForge, F. B., et al., Chemical Reviews 12: 181, 1933.

1890. LaForge, F. B., et al., Journal of the American Chemical Society 70: 3707, 1948.

1891. Ibid., 74: 5392, 1952.

1892. LaForge, F. B., et al., The Journal of Organic Chemistry (Baltimore) 17: 381, 1952.

1893. LaForge, F. B., and Barthel, W. F., The Journal of Organic Chemistry (Baltimore) 9: 242, 1944.

1894. Ibid., 10: 106, 1945.

1895. Ibid., 10: 114, 1945.

1896. Ibid., 10: 222, 1945.

1897. Ibid., 12: 199, 1947.

1898. LaForge, F. B., and Green, N., The Journal of Organic Chemistry 17: 1635, 1952.

1899. LaForge, F. B., and Markwood, L. W., Annual Review of Biochemistry 7: 473, 1938.

1900. Lalatta, F., Rivista di Frutticoltura (Ravenna, Italia) 14: 159, 1952.

1901. Lalonde, D., and Brown, A. W. A., Canadian Journal of Zoölogy 32: 74, 1954.

1902. Lamson, P. D., The Journal of Pharmacology and Experimental Therapeutics 22: 215, 1923.

1903. Lamson, P. D., et al., The American Journal of Hygiene 9: 430, 1929.

1904. Lancaster, J. L., The Journal of Economic Entomology 44(5): 718, 1951.

1905. Landauer, W., Journal of Agricultural Research (Washington, D.C.) 43: 67, 1931.
1906. Landé, K. E., and Boone, G., The Journal of the American Medical Association 153: 179, 1953.
1907. Lande, P., Archives des maladies professionelles; hygiène et toxicologie industrielles (Paris) 2: 454, 1939.
1908. Lane, R. L., and Williams, R. J., Archives of Biochemistry (New York) 19: 329, 1948.
1909. Lane, R. L., The Journal of Biological Chemistry (Baltimore) 163: 251, 1946.
1910. Lange, W. H., California Agricultural Experiment Station Circular No. 365, 1946.
1911. Lange, W. H., The Journal of Economic Entomology 38: 643, 1945.
1912. Lange, W. H., et al., The Journal of Economic Entomology 42: 942, 1949.
1913. Lange, W. H., and Smith, L. M., The Journal of Economic Entomology 40: 496, 1947.
1914. Langford, G. S., The Journal of Economic Entomology 46(2): 262, 1953.
1915. Langford, G. S., et al., The Journal of Economic Entomology 47(3): 438, 1954.
1916. Langhorst, H. J., Agricultural Chemicals 2(4): 30, 1947.
1917. Langhorst, H. J., American Cyanamid Company, Circular Letter, October 17, 1949.
1918. Langley, J. N., and Dickinson, W. L., The Journal of Physiology 11: 265, 1890.
1919. Largent, E. J., Archives of Industrial Hygiene and Occupational Medicine 6: 37, 1952.
1920. Largent, E. J., and Heyroth, F. F., The Journal of Industrial Hygiene and Toxicology 31: 134, 1949.
1921. Larson, P. S., The Journal of Pharmacology and Experimental Therapeutics 77: 343, 1943.
1922. Larson, P. S., et al., The Journal of Pharmacology and Experimental Therapeutics (in press).
1923. Ibid., 95: 506, 1949.
1924. Latta, R., and Johnson, A. C., The Journal of Economic Entomology 37: 261, 1944.
1925. Latta, R., and Lane, C., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
1926. Laudani, H., and Marske, F. O., The Journal of Economic Entomology 42: 434, 1949.
1927. Laug, E. P., The Journal of Pharmacology and Experimental Therapeutics 86: 324, 332, 1946.
1928. Ibid., 93: 277, 1948.
1929. Laug, E. P., et al., Archives of Industrial Hygiene and Occupational Medicine 3: 245, 1951.
1930. Laug, E. P., et al., The Journal of Pharmacology and Experimental Therapeutics 98: 268, 1950.
1931. Laug, E. P., and Fitzhugh, O. G., The Journal of Pharmacology and Experimental Therapeutics 87: 18, 1946.
1932. Laug, E. P., and Kunze, F. M., Federation Proceedings 10: 318, 1951.
1933. Lauger, P. H., et al., Helvetica chimica acta (Basel) 27: 892, 1944.
1934. Lauger, P. H., et al., Helvetica physiologica et pharmacologica acta (Basel) 3: 405, 1945.
1935. Lauger, P. H., et al., "Mechanism of Intoxication of DDT Insecticides, J. A. Geigy Company, New York, 1946.
1936. Lawless, J. J., The West Virginia Medical Journal (Charleston) 46: 125, 1950.
1937. Lawrence, H. M., Progressive Fish-Culturist 12(3): 141, 1950.
1938. Lazarew, N. W., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 141: 19, 1929.
1939. Leach, B. R., Journal of Agricultural Research (Washington, D.C.) 33: 1, 1926.
1940. Leach, B. R., and Lipp, J. W., United States Golf Association, Greens Section Bulletin No. 6, 1926.
1941. Leake, C. D., The Journal of Pharmacology and Experimental Therapeutics 33: 279, 1928.
1942. Leake, C. D., and Ritchie, B., The American Journal of Physiology 76: 234, 1926.
1943. Lear, B., Cornell University Agricultural Experiment Station Bulletin No. 850, 1948.
1944. Lear, B., and Newhall, A. G., Phytopathology 38: 38, 1948.
1945. Leclerc, E., and Devlaminck, F., Centre Belge d'Etude et de Documentation des Eaux (Université de Liège), Bulletin (Place du Vingt Aout, Liège) 14: 246, 1951.
1946. Lecointe, P., Revue de botanique appliquée et d'agriculture tropicale (Paris, Laboratoire d'agronomie coloniale) 16: 609, 1936.
1947. LeGoupil, Revue de pathologie végétale et d'entomologie agricole (Paris) 19: 169, 1932.
1948. Lehman, A. J., Blue Book (Soap and Sanitary Chemicals) 21st Edition, 1949, p. 173.
1949. Lehman, A. J., Quarterly Bulletin of the Association of Food and Drug Officials of the United States 12: 82, 1948.
1950. Ibid., 14: 82, 1950.
1951. Ibid., 15: 122, 1951.
1952. Ibid., 16: 3, 1952.
1953. Ibid., 16: 47, 1952.
1954. Ibid., 16: 85, 1952.
1955. Ibid., 16: 126, 1952.
1956. Lehman, R. S., The Journal of Economic Entomology 23: 958, 1930.
1957. Ibid., 26: 1042, 1933.
1958. Ibid., 35(5): 659, 1942.
1959. Lehmann, C., Zeitschrift für Fischerei und deren Hilfswissenschaften 24: 1926.
1960. Lehmann, K. B., Archiv für Hygiene und Bakteriologie (Munchen) 20: 26, 1894.
1961. Ibid., 74: 1, 1911.
1962. Ibid., 75: 1, 1912.
1963. Lehmann, K. B., and Schmidt-Kehl, L., Archiv für Hygiene und Bakteriologie (München) 116: 131, 1936.
1964. Leighton, R. E., et al., Journal of Dairy Science 35: 214, 1952.
1965. Lejeune, E., Schweizerische medizinische Wochenschrift (Basel) 66: 914, 1936.
1966. Lemmon, A. B., Citrus Leaves 29: 6, 1949.
1967. Lendle, L., and Schneider, H. H., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 210: 119, 1950.
1968. Lendle, L., and Schneider, H. H., Klinische Wochenschrift (Berlin) 29: 388, 1951.
1969. Lennox, F., Australia, Council for Scientific and Industrial Research Pamphlet No. 101, 1940.
1970. Lensky, P., and Evans, L., The Journal of the American Medical Association 149: 1394, 1952.
1971. Leonard, C. S., The Journal of Economic Entomology 35(2): 261, 1942.
1972. Leonard, J. W., Transactions. The American Fisheries Society 68: 269, 1938.
1973. Lepesme, P., Comptes rendus hebdomadaires des séances de l'Académie des sciences (Paris) 204: 717, 1937.

1974. LeRoux, E. J., and Morrison, F. O., The Journal of Economic Entomology 46(6): 1109, 1953.
1975. Ibid., 47(6): 1058, 1954.
1976. Lesser, M. A., Soap and Sanitary Chemicals 25: 133, 1949.
1977. Létard, H., and DeSacy, G. S., Comptes rendus des séances de la Société de biologie (Paris) 139: 353, 1945.
1978. Leukel, R. W., Phytopathology 30: 274, 1940.
1979. Leuze, E., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 95: 145, 1922.
1980. Levene, and Suran, Nature (London) 166: 698, 1950.
1981. Lewallen, L. L., The Journal of Economic Entomology 47(6): 1137, 1954.
1982. Lewin, Archiv für pathologische Anatomie und Physiologie, und für klinische Medizin 78: 113, 1879.
1983. Lewis, S. E., Nature (London) 161: 692, 1948.
1984. Ibid., 172: 1004, 1953.
1985. Lewis, S. E., and Eccleston, K., Journal of the Society of Chemical Industry (London) 65(5): 149, 1946.
1986. Lhoste, J., and Leibovici, C., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris, 1952, p. 474.
1987. Lickerish, L. A., Journal of the Science of Food and Agriculture 4: 24, 1953.
1988. Lidov, R., et al., Advances in Chemistry Series 1: 175, 1950.
1989. Lieben, J., and Waldman, J. K., Archives of Industrial Hygiene and Occupational Medicine 7: 93, 1953.
1990. Lienk, S. E., and Chapman, P. J., The Journal of Economic Entomology 46(6): 1085, 1953.
1991. Liese, Zeitschrift für hygienische Zoologie und Schädlingsbekämpfung (Berlin) 33: 1, 1941.
1992. Lightbody, H., and Matthews, J., Industrial and Engineering Chemistry 28: 809, 1936.
1993. Liles, J. N., and Fisk, F. W., The Journal of Economic Entomology 48(2): 217, 1955.
1994. Lillie, R. D., et al., Archives of Pathology (Chicago) 43: 127, 1947.
1995. Lillie, R. D., and Smith, M. I., Public Health Reports (Washington, D.C.) 59: 979, 1944.
1996. Lilly, J. H., Annual Review of Entomology 1: 203, 1956.
1997. Lilly, J. H., The Journal of Economic Entomology 47(4): 651, 1954.
1998. Lilly, J. H., The National Fertilizer Review 30: 3, 1955.
1999. Lincoln, C. J., et al., The Journal of Economic Entomology 35: 238, 1942.
2000. Lindebaum, A., et al., The Journal of Biological Chemistry (Baltimore) 190: 585, 1951.
2001. Lindeman, V. F., and Burlington, H., Federation Proceedings 10: 85, 1951.
2002. Lindgren, D. L., Hilgardia 13: 491, 1941.
2003. Lindgren, D. L., Minnesota Agricultural Experiment Station Technical Bulletin No. 109, 1935.
2004. Lindgren, D. L., et al., The Journal of Economic Entomology 47(4): 705, 1954.
2005. Ibid., 47(5): 923, 1954.
2006. Lindgren, D. L., and Dickson, R. C., The Journal of Economic Entomology 38(3): 296, 1945.
2007. Lindgren, D. L., and Gerhardt, P. D., The Journal of Economic Entomology 40: 680, 1947.
2008. Lindgren, D. L., and Shepard, H. H., The Journal of Economic Entomology 25: 248, 1932.
2009. Lindgren, D. L., and Vincent, L. E., The Journal of Economic Entomology 44(6): 975, 1951.
2010. Lindquist, A. W., et al., The Journal of Economic Entomology 37(1): 132, 1944.
2011. Ibid., 38(2): 261, 1945.
2012. Ibid., 40: 426, 1947.
2013. Ibid., 44(1): 167, 1951.
2014. Ibid., 44: 572, 1951.
2015. Ibid., 44: 931, 1951.
2016. Lindquist, A. W., et al., Journal of the Kansas Entomological Society 19: 13, 1946.
2017. Lindquist, A. W., et al., U.S. Department of Agriculture Bulletin No. E-755, 1949.
2018. Lindquist, A. W., and Bushland, R., The Journal of Economic Entomology 37(6): 842, 1944.
2019. Lindquist, A. W., and Roth, A. R., The Journal of Economic Entomology 43: 328, 1950.
2020. Lindquist, A. W., and Smith, C. N., Contributed Data, 1954.
2021. Lindquist, A. W., and Wilson, H. G., Science 107: 276, 1948.
2022. Lindquist, D. A., and Dahm, P. A., The Journal of Economic Entomology 49(5): 579, 1956.
2023. Linduska, J. P., et al., The Journal of Economic Entomology 39: 767, 1946.
2024. Ibid., 41(1): 43, 1948.
2025. Linduska, J. P., et al., Special Scientific Report on Wildlife No. 9, 1951. (U.S. Fish and Wildlife Service, Washington, D.C.).
2026. Linduska, J. P., and Surber, E. W., U.S. Fish and Wildlife Service, Circular No. 15, 1948.
2027. Lipp, J. W., The Journal of Economic Entomology 22: 600, 1929.
2028. List, G. M., and Hoerner, J. L., The Journal of Economic Entomology 40: 138, 1947.
2029. Litzenberger, S. C., et al., Montana Agricultural Experiment Station Bulletin No. 426, 1945.
2030. Livingstone, E. M., and Swank, G. R., The Journal of Economic Entomology 35: 919, 1942.
2031. Lochhead, H. B., and Close, H. P., The Journal of the American Medical Association 146: 1322, 1951.
2032. Lockard, D. H., Data contributed on behalf of the Holcomb Manufacturing Company in 1955, (data dated September, 1953).
2033. Lockard, D. H., and Fisk, F. W., The Journal of Economic Entomology 46(1): 20, 1953.
2034. Lockaw, S., and Ludicke, M., Zeitschrift für Naturforschung (Wiesbaden) 7b: 389, 1952.
2035. Loechner, E. H., Department of Agriculture of South Africa (Union of) Scientific Bulletin No. 333, 1952, p. 14.
2036. Loomis, W. F., and Lipmann, F., The Journal of Biological Chemistry (Baltimore) 173: 807, 1948.
2037. Loosanoff, V. L., Fishing Gazette 64(4): 94, 1947.
2038. Lord, F. T., The Canadian Entomologist 79: 196, 1947.
2039. Ibid., 81: 202; 217, 1949.
2040. Lord, K. A., Annals of Applied Biology 35(4): 505, 1948.
2041. Ibid., 36: 113, 1949.
2042. Ibid., 37: 105, 1950.
2043. Lord, K. A., and Potter, C., Annals of Applied Biology 38: 495, 1951.
2044. Lord, K. A., and Potter, C., Journal of the Science of Food and Agriculture 5: 490, 1954.
2045. Lord, K. A., and Potter, C., Nature (London) 172: 679, 1953.

2046. Louis, R., Oestereichische Bauern Bündler 70: 10, 1951.
2047. Lowenstein, O., Nature (London) 150: 760, 1942.
2048. Lubatti, O. F., Journal of the Society of Chemical Industry (London) 55: 344, 1936.
2049. Lucas, G. H. W., The Journal of Pharmacology and Experimental Therapeutics 34: 223, 1934.
2050. Ludewig, S., and Chanutin, A., Proceedings of the Society for Experimental Biology and Medicine 62: 20, 1946.
2051. Ludvik, G. F., The Journal of Economic Entomology 46(2): 364, 1953.
2052. Ludvik, G. F., et al., The Journal of the National Malaria Society (Tallahassee, Florida) 10: 23, 1951.
2053. Ludvik, G. F., and Decker, G. C., The Journal of Economic Entomology 40(1): 97, 1947.
2054. Ibid., 44(3): 405, 1951.
2055. Ludwig, D., Annals of the Entomological Society of America 39: 496, 1946.
2056. Ludzack, T. J., et al., Sewage Works Journal 18: 678, 1946.
2057. Lusis, E., Höfchen-Briefe für Wissenschaft und Praxis (Bayer Pflanzenschutz Nachrichten) 5: 225, 1952.
2058. Luther, H., et al., Zeitschrift für Naturforschung (Wiesbaden) 4: 133, 1949.
2059. Lutz, G., Archiv für Gewerbepathologie und Gewerbehygiene (Berlin) 1: 741, 1930.
2060. Lyte, C., and Fortune, I., The Journal of Economic Entomology 41: 833, 1948.
2061. Machle, W., et al., The Journal of Industrial Hygiene and Toxicology 24: 199, 1942.
2062. Ibid., 25: 192, 1943.
2063. Ibid., 27: 95, 1945.
2064. Macht, The Journal of Pharmacology and Experimental Therapeutics 50: 93, 1934.
2065. Mackenthum, K. M., Sewage and Industrial Wastes 22: 1062, 1950.
2066. Mackerras, I. M., and West, R. F. K., The Medical Journal of Australia (Sydney) 1: 400, 1946.
2067. Mackie, D. B., The Journal of Economic Entomology 31(1): 70, 1938.
2068. Mackie, D. B., and Carter, W. B., California Department of Agriculture Bulletin 26: 153, 1937.
2069. Mackworth, J., and Webb, E., Biochemical Journal (London) 42: 91, 1948.
2070. MacLeod, G. F., Proceedings of the Thirteenth National Shade Tree Conference, 1937.
2071. MacLeod, J., Annals of Applied Biology 34: 207, 1947.
2072. Madden, A. H., et al., The Journal of Economic Entomology 37(1): 127, 1944.
2073. Madsen, H. F., and Borden, A. D., The Journal of Economic Entomology 42: 915, 1949.
2074. Madsen, L. L., U.S. Department of Agriculture Yearbook 1942, p. 645.
2075. Maelzer, D., and Kirk, R., Australian Journal of Biological Sciences 6: 244, 1953.
2076. Magee, W. J., and Gaines, J. C., The Journal of Economic Entomology 43(3): 281, 1950.
2077. Magy, H., and Hoskins, W. H., The Journal of Economic Entomology 38: 524, 1945.
2078. Main, R., and Haag, H., Industrial Medicine 11: 531, 1942.
2079. Mally, C. W., South Africa Department of Agriculture Journal 6: 220, 1923.
2080. Mangan, G. F., Thesis; Georgetown University, Washington, D.C., 1954.
2081. Mangun, G. H., and DuBois, K. P., Federation Proceedings 6: 353, 1947.
2082. Manis, H. C., et al., The Journal of Economic Entomology 35(5): 662, 1942.
2083. Manson, D., The Indian Medical Gazette (Calcutta) 69: 500, 1934.
2084. Manville, I. A., The American Journal of Public Health 29: 709, 1939.
2085. Maplestone, P. A., and Chopra, R. M., The Indian Medical Gazette (Calcutta) 68: 554, 1933.
2086. Maplestone, P. A., and Mukerji, A. K., The Indian Medical Gazette (Calcutta) 72: 650, 1937.
2087. Maqsud. Nasir, N., Journal of the Science of Food and Agriculture 4: 374, 1953.
2088. Marais, et al., Farming in South Africa, 1950 quoted by Brown, A. W. A. in "Insect Control by Chemicals".
2089. March, R. B., Thesis; University of Illinois, 1949.
2090. March, R. B., The Journal of Economic Entomology 45: 452, 1952.
2091. March, R. B., et al., The Journal of Economic Entomology 45: 851, 1952.
2092. Ibid., 49(2): 185, 1956.
2093. March, R. B., and Lewallen, L., The Journal of Economic Entomology 43: 670; 721, 1950.
2094. March, R. B., and Metcalf, R. L., California Department of Agriculture Bulletin 37: 93, 1949.
2095. March, R. B., and Metcalf, R. L., Pest Control 20: 12; 14; 16; 18, 1952.
2096. March, R. B., and Metcalf, R. L., Soap and Sanitary Chemicals 26(7): 121, 1950.
2097. Ibid., 26(7): 123; 125; 139, 1950.
2098. March, R. B., and Metcalf, R. L., University of California Citrus Experiment Station Newsletter No. 38, 1949.
2099. Marchand, J. F., The Journal of the American Medical Association 149: 738, 1952.
2100. Marcovitch, S., The Journal of Economic Entomology 21: 108, 1928.
2101. Marcovitch, S., The Journal of Pharmacology and Experimental Therapeutics 34: 179, 1928.
2102. Marcovitch, S., et al., Tennessee Agricultural Experiment Station Bulletin No. 162, 1937.
2103. Marcovitch, S., and Anthony, M. V., The Journal of Economic Entomology 24: 490, 1931.
2104. Marcovitch, S., and Stanley, W. W., Tennessee Agricultural Experiment Station Bulletin No. 140, 1929.
2105. Ibid., Bulletin No. 174, 1941.
2106. Ibid., Bulletin No. 195, 1945.
2107. Markwood, L., Science 92: 204, 1940.
2108. Markwood, L., U.S. Department of Agriculture Bureau of Entomology and Plant Quarantine No. E-561, 1942.
2109. Marsh, H., Montana Agricultural Experiment Station Bulletin No. 461, 1949.
2110. Marsh, M. W., and Eden, W. G., The Journal of Economic Entomology 48(5): 610, 1955.
2111. Marshall, D. S., et al., The Journal of Economic Entomology 42: 315, 1949.
2112. Marshall, G. E., The Journal of Economic Entomology 43: 164, 1950.
2113. Marshall, J., The Journal of Economic Entomology 32: 838, 1939.
2114. Ibid., 41: 592, 1948.
2115. Marshall, J., Scientific Agriculture (Canada, Dominion of) 25: 546, 1945.
2116. Marshall, J., and Groves, K., The Journal of Economic Entomology 29: 658, 1936.

2117. Martin, H., Annals of Applied Biology 22: 334, 1935.
2118. Ibid., 36: 153, 1949.
2119. Martin, H., Annual Review of Entomology 1: 149, 1956.
2120. Martin, H., "Guide to the Chemicals Used in Crop Protection", (mimeograph) 2nd Edition, University of Western Ontario, London, Ontario, 1955.
2121. Martin, H., Journal of the Science of Food and Agriculture 6: 163, 1950.
2122. Martin, H., Journal of the Society of Chemical Industry (London) 50: 91, 1931.
2123. Ibid., 65: 402, 1946.
2124. Martin, H., Research (London) 1: 640, 1948.
2125. Martin, H., "Scientific Principles of Crop Protection", 1940, p. 117.
2126. Martin, H., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, Volume II, p. 303.
2127. Martin, H., et al., Annual Report of the University of Bristol Long Ashton Research Station (Great Britain) 1943, p. 62.
2128. Martin, H., and Shaw, H., British Intelligence Objectives Sub-Committee Report No. 1095, item 22, 1946. H. M. Stationery Office, London.
2129. Martin, H., and Wain, R., Annual Report of the Agricultural and Horticultural Research Station, Long Ashton, Bristol (Great Britain) 1944, p. 12.
2130. Martin, J. T., Annals of Applied Biology 27: 274, 1940.
2131. Ibid., 29: 62, 1942.
2132. Martin, J. T., and Hester, K. H. C., The British Journal of Dermatology and Syphilis (London) 53: 127, 1941.
2133. Mason, A. C., et al., The Journal of Economic Entomology 36: 734, 1943.
2134. Mason, A. C., and Chisholm, R. D., The Journal Of Economic Entomology 38: 717, 1945.
2135. Mathis, W., and Quarterman, K. D., The American Journal of Tropical Medicine and Hygiene 2: 318, 1953.
2136. Matsubara, H., Botyu Kagaku (Kyoto) 17: 143, 1952.
2137. Matsubara, H., Science (Japan) 20: 183, 1950.
2138. Matsui, M., et al., Journal of the American Chemical Society 74: 2181, 1952.
2139. Matsui, M., Japanese Patent No. 2119, (1952).
2140. Mattson, A. M., et al., Journal of Agricultural and Food Chemistry 3(4): 319, 1955.
2141. Mattson, A. M., et al., 126th Meeting of the American Chemical Society, New York 1954, Abstract.
2142. Maurice, H. G., Bulletin of Hygiene (London) 6: 74, 1931.
2143. Maxwell, C. W. B., 78th Annual Report of the Entomological Society of Ontario (Canada, Dominion of,) 1947, p. 51.
2144. May and Baker, Limited, "Fumigation with Methyl Bromide", Dagenham (Great Britain).
2145. May, A. W. S., and Fisher-Webster, K., The Queensland Agricultural Journal (Australia) 67: 143, 1948.
2146. Mayer, E., et al., The Journal of Economic Entomology 44: 946, 1953.
2147. Mayer, Comptes rendus hebdomadaires des séances de l'Académie des sciences (Paris) 171: 1396, 1920.
2148. Mayeux, H. S., and Wene, G., The Journal of Economic Entomology 43(6): 908, 1951.
2149. Mazur, A., The Journal of Biological Chemistry (Baltimore) 164: 271, 1946.
2150. Mazur, A., and Bodansky, O., The Journal of Biological Chemistry (Baltimore) 163: 261, 1946.
2151. McAllister, L. C., et al., The Journal of Economic Entomology 40: 905, 1947.
2152. McAllister, L. C., and Van Leeuwen, E. R., The Journal of Economic Entomology 23(6): 907, 1930.
2153. McArdle, The Quarterly Journal of Medicine 9: 107, 1940.
2154. McCallan, S. E. A., and Weedon, F. R., Contributions from the Boyce Thompson Institute 11: 331, 1940.
2155. McCance, et al., Biochemical Journal (London) 45: 493, 1949.
2156. McCance, and Jones, Biochemical Journal (London) 45: 464, 1949.
2157. McCombie, H., and Saunders, B. C., Nature (London) 157: 287, 1946.
2158. Ibid., 158: 382, 1946.
2159. McCord, C. P., American Journal of Public Health 24: 677, 1934.
2160. McCord, C. P., The Journal of the American Medical Association 99: 409, 1932.
2161. McCrone, W., U.S. Patent No. 2,393,999 (1946).
2162. McCulloch, R. N., Journal of the American Veterinary Medical Association 96: 321, 1940.
2163. McCulloch, R. N., The Medical Journal of Australia (Sydney) 1: 449, 1947.
2164. McDaniel, E., Michigan Agricultural Experiment Station Circular No. 94, 1926.
2165. McDonald, G., British Medical Bulletin (London) 3: 218, 1945.
2166. McDuffie, W. C., et al., The Journal of Economic Entomology 39: 743, 1946.
2167. Ibid., 43: 520, 1950.
2168. McDuffie, W. C., et al., Mosquito News 9: 145, 1949.
2169. McEwen, F. L., and Chapman, R. K., The Journal of Economic Entomology 45(4): 717, 1952.
2170. McGavack, The Journal of Industrial Hygiene and Toxicology 23: 239, 1941.
2171. McGee, L. C., and Reed, H. L., The Journal of the American Medical Association 149: 1124, 1952.
2172. McGovran, E. R., Annals of the Entomological Society of America 35: 23, 1942.
2173. McGovran, E. R., The Journal of Economic Entomology 25: 271, 1934.
2174. McGovran, E. R., Journal of the New York Entomological Society 37: 513, 1929.
2175. McGovran, E. R., Thesis; Iowa State College, 1933.
2176. McGovran, E. R., et al., The Journal of Economic Entomology 33: 525, 1940.
2177. Ibid., 36(5): 732, 1943.
2178. McGovran, E. R., et al., U.S. Department of Agriculture Bureau of Entomology and Plant Quarantine No. E-544, 1941.
2179. McGovran, E. R., and Piquett, P. G., The Journal of Economic Entomology 36(6): 936, 1943.
2180. Ibid., 38: 936, 1945.
2181. McGovran, E. R., and Piquett, P. G., Soap and Sanitary Chemicals 22(8): 157, 1946.
2182. McGregor, E. A., The Journal of Economic Entomology 37(1): 78, 1944.
2183. McGregor, W. S., The Journal of Economic Entomology 42: 641, 1949.

2184. McGregor, W. S., and Bushland, R. C., The Journal of Economic Entomology 49(1): 86, 1956.
2185. McGregor, W. S., and Radeleff, R. D., The Journal of Economic Entomology 47(3): 465, 1954.
2186. McIlwain, H., The British Journal of Experimental Pathology (London 23: 95, 1942.
2187. McIndoo, N. E., Journal of Agricultural Research (Washington, D.C.) 7: 89, 1916.
2188. Ibid., 55(12): 909, 1937.
2189. McIndoo, N. E., U.S. Department of Agriculture Bureau of Entomology and Plant Quarantine No. E-392, 1936.
2190. Ibid., No. E-661, 1945.
2191. Ibid., No. E-666, 1945.
2192. McIndoo, N. E., and DeMuth, G. S., U.S. Department of Agriculture Bulletin No. 1364, 1926.
2193. McIndoo, N. E., and Sievers, A. F., U.S. Department of Agriculture Publication No. 1201, 1924.
2194. McIntosh, A. H., Annals of Applied Biology 34: 586, 1947.
2195. Ibid., 36: 535, 1949.
2196. Ibid., 38: 567, 1951.
2197. Ibid., 38: 881, 1951.
2198. McKenzie, R. E., and Hoskins, W. M., The Journal of Economic Entomology 47(6): 984, 1954.
2199. McLaine, L. S., and Monro, H. A. U., 67th Annual Report of the Entomological Society of Ontario (Canada, Dominion of), 1936.
2200. McLaughlin, R. M., Quarterly Bulletin of the Association of Food and Drug Officials of the United States 15: 67, 1951.
2201. McLean, H. C., et al., The Journal of Economic Entomology 37(2): 315, 1944.
2202. McLeod, W. S., Department of Agriculture (Canada, Dominion of) Division of Entomology, 1949, "Review of Literature on Systemic Insecticides".
2203. McLeod, W. S., Fruit Insect Unit (Ottawa, Canada) Scientific Service Research Notes, Series E-6, 1951.
2204. McLeod, W. S., The Journal of Economic Entomology 39: 815, 1946.
2205. McLure, F., "Trace Elements in Nutrition", in "Handbook of Nutrition", 2nd Edition, American Medical Association, 1951.
2206. McNamara, B. P., Federation Proceedings 6: 357, 1947.
2207. McNamara, B. P., et al., Federation Proceedings 5: 67, 1946.
2208. McNamara, B. P., and Krop, S., The Journal of Pharmacology and Experimental Therapeutics 92: 140, 1948.
2209. Ibid., 92: 147, 1948.
2210. McOmie, The Journal of Industrial Hygiene and Toxicology 31: 113, 1949.
2211. Medler, J. T., and Scholl, J. M., The Journal of Economic Entomology 40: 579, 1947.
2212. Meerssman, F., et al., Comptes rendus de la Société de biologie (Paris) 117: 934, 1934.
2213. Melander, A. L., The Journal of Economic Entomology 7: 167, 1914.
2214. Mellanby, K., Proceedings of the Royal Society (London) B116: 139, 1934.
2215. Meltzer, J., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, Volume II, p. 987.
2216. Melvin, R., The Journal of Economic Entomology 41(6): 903, 1948.
2217. Mendel, et al., Biochemical Journal (London) 37: 473, 1943.
2218. Mendel, and Rudney, Science 100: 499, 1944.
2219. Menusan, H., The Journal of Economic Entomology 41(2): 302, 1948.
2220. Menusan, H., and Heal, R., The Journal of Economic Entomology 41(4): 535, 1948.
2221. Merck (The) Index, 6th Edition.
2222. Merkl, M. E., and Dunnam, E. W., The Journal of Economic Entomology 47(5): 869, 1954.
2223. Merrell, D. J., and Underhill, J. C., The Journal of Economic Entomology 49(3): 300, 1956.
2224. Merrill, R., et al., The Journal of Cellular and Comparative Physiology 28: 465, 1946.
2225. Merzbach, E., Zeitschrift für die gesamte experimentelle Medizin (Berlin) 63: 383, 1928.
2226. Metcalf, R. H., and Flint, "Useful and Destructive Insects", McGraw-Hill, New York, 1951.
2227. Metcalf, R. L., The Journal of Economic Entomology 40: 522, 1947.
2228. Ibid., 41(1): 194, 1948.
2229. Ibid., 41(3): 416, 1948.
2230. Ibid., 41(6): 875, 1948.
2231. Metcalf, R. L., "Organic Insecticides", Interscience, New York, 1955.
2232. Metcalf, R. L., "Organic Insecticides", quoting others; modified to correct errors.
2233. Metcalf, R. L., Physiological Review 35: 197, 1955.
2234. Metcalf, R. L., Science 108: 84, 1948.
2235. Metcalf, R. L., et al., Journal of Agricultural and Food Chemistry 3(12): 1011, 1955.
2236. Metcalf, R. L., et al., The Journal of Economic Entomology 47(6): 1045, 1954.
2237. Ibid., 48(4): 355, 1955.
2238. Ibid., 48(4): 364, 1955.
2239. Ibid., 49(6): 738, 1956.
2240. Metcalf, R. L., and Gunther, F., Journal of the American Chemical Society 69: 2579, 1947.
2241. Metcalf, R. L., and Kearns, C. W., The Journal of Economic Entomology 34(2): 306, 1941.
2242. Metcalf, R. L., and Lindgren, D. L., The Journal of Economic Entomology 41(3): 522, 1948.
2243. Metcalf, R. L., and March, R. B., Annals of the Entomological Society of America 46: 63, 1953.
2244. Metcalf, R. L., and March, R. B., The Journal of Economic Entomology 42(5): 721, 1949.
2245. Ibid., 43(5): 670, 1950.
2246. Ibid., 45(6): 988, 1952.
2247. Ibid., 46(2): 288, 1953.
2248. Metcalf, R. L., and March, R. B., Science 117: 527, 1953.
2249. Metcalfe, C. R., Annals of Applied Biology 28: 301, 1941.
2250. Metzger, F. G., Industrial and Engineering Chemistry 18: 161, 1926.
2251. Michael, A. S., et al., Science 123(3194): 464, 1956.
2252. Michaelis, A., Liebigs Annalen No. 326, p. 129, 1903.
2253. Ibid., No. 407, p. 290, 1915.
2254. Michaelis, M., et al., The American Journal of Physiology 157: 463, 1949.
2255. Michel, H., Biochemical Journal (London) 54: xxiv, 1953.
2256. Michelbacher, A. E., The Journal of Economic Entomology 48(5): 504, 1955.
2257. Michelbacher, A. E., et al., The Journal of Economic Entomology 43: 448, 1950.
2258. Ibid., 47(2): 366, 1954.

2259. Middlekauff, W. W., and Hansberry, R., The Journal of Economic Entomology 34(5): 625, 1941.

2260. Middleton, W., and Cronin, T. C., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.

2261. Mikalonis, S., and Brown, R., The Journal of Cellular and Comparative Physiology 18: 401, 1941.

2262. Mikeska, L., U.S. Patent No. 2,637,676, (1953).

2263. Milani, R., First International Symposium on the Control of the Insect Vectors of Disease, 1954, p. 253.

2264. Miles, H. W., Annals of Applied Biology 14: 240, 1927.

2265. Milks, H. J., "Veterinary Pharmacology, Materia Medica and Therapeutics", 5th Edition, Alexander Eger, Chicago 1943, p. 323.

2266. Miller, A., et al., The Journal of Economic Entomology 45(1): 94, 1952.

2267. Miller, D. P., and Haggard, H. W., The Journal of Industrial Hygiene and Toxicology 25: 423, 1943.

2268. Miller, J. T., and Byers, H. G., Journal of the American Water Works Association 28: 1159, 1936.

2269. Miller, R. L., et al., U.S. Department of Agriculture Technical Bulletin No. 350, 1933.

2270. Milles, H. L., and Salt, H. B., The British Medical Journal (London) 2: 444, 1950.

2271. Ministry of Agriculture and Fisheries, Fisheries Notice No. 28, 1949 (Water Pollution Abstracts 22: July, 1949).

2272. Ministry of Food, Food Standards Committee, Water Pollution Abstracts 23: February, 1950.

2273. Mises, R., Thèse, Paris, 1951.

2274. Missiroli, A., Rivista di parassitologia (Roma, Italia) 8: 141, 1947.

2275. Missonier, J., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952, p. 480.

2276. Mistric, W. J., and Rainwater, C. F., The Journal of Economic Entomology 43(6): 892, 1950.

2277. Ibid., 45(1): 76, 1952.

2278. Mitchell, R. T., et al., Journal of Wildlife Management 17: 45, 1953.

2279. Mitchener, A. V., The Journal of Economic Entomology 42(1): 152, 1949.

2280. Ibid., 43(1): 176, 1950.

2281. Ibid., 44(1): 66, 1951.

2282. Ibid., 46(1): 164, 1953.

2283. Ibid., 46(6): 1118, 1953.

2284. Mitlin, N., The Journal of Economic Entomology 49(5): 683, 1956.

2285. Mitlin, N., et al., The Journal of Economic Entomology 49(4): 544, 1956.

2286. Mitlin, N., et al., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine, No. E-865, 1953.

2287. Mitlin, N., and Konecky, M., The Journal of Economic Entomology 48(1): 93, 1955.

2288. Modern Drug Encyclopedia (The)

2289. Molnar, N. M., Soap and Sanitary Chemicals 23(7): 143, 1947.

2290. Monroe, E., and Hand, C., Journal of the American Chemical Society 72: 5345, 1950.

2291. Moore, J. B., The Journal of Economic Entomology 43(2): 207, 1950.

2292. Ibid., 43(2): 213, 1950.

2293. Moore, W., Journal of Agricultural Research (Washington, D.C.) 9: 371, 1916.

2294. Ibid., 10: 365, 1917.

2295. Moore, W., The Journal of Economic Entomology 9: 71, 1916.

2296. Moore, W., The Journal of Laboratory and Clinical Medicine 3: 261, 1918.

2297. Moore, W., and Carpenter, E. L., The Journal of Economic Entomology 31(3): 419, 1938.

2298. Moore, W., and Graham, S.A., The Journal of Economic Entomology 11(1): 70, 1918.

2299. Moorefield, H., and Kearns, C. W., The Journal of Economic Entomology 48(2): 403, 1955.

2300. Morrill, A. W., The Journal of Economic Entomology 14: 394, 1921.

2301. Morris, H. E., and Swingle, D. B., Journal of Agricultural Research (Washington, D.C.) 34: 59, 1927.

2302. Morrison, F. O., 80th Annual Report of the Entomological Society of Ontario (Canada, Dominion of) 1950, p. 50.

2303. Morrison, F. O., and Olwer, W. F., Canadian Journal of Research D27: 265, 1949.

2304. Morrison, H. E., et al., The Journal of Economic Entomology 41(3): 374, 1948.

2305. Morrison, P. E., and Brown, A. W. A., The Journal of Economic Entomology 47(5): 723, 1954.

2306. Morse, A. P., The Journal of Economic Entomology 3: 104, 1910.

2307. Morse, H. H., Soil Science 39: 177, 1935.

2308. Mountain, J. T., et al., Industrial Health Monthly 11: 88, 1951. (now titled Occupational Health)

2309. Mounter, and Whittaker, Biochemical Journal (London) 47: 525, 1950.

2310. Moxon, L. A., and Rhian, M., Physiological Review 23: 305, 1943.

2311. Mudge, G. H., and Taggart, J. V., The American Journal of Physiology 161: 173, 1950.

2312. Muehlberger, C. W., The Journal of Pharmacology and Experimental Therapeutics 39: 246, 1930.

2313. Mühlens, K., Duetsche medizinische Wochenschrift (Leipzig) 71: 164, 1946.

2314. Mühlmann, H., Höfchen-Briefe für Wissenschaft und Praxis (Bayer Pflanzenschutz Nachrichten) 6: 73, 1953.

2315. Müller, J., Archiv für experimentelle Pathologie und Pharmakologie 109: 276, 1925.

2316. Müller, I., Archiv für Gewerbepathologie und Gewerbehygiene (Berlin) 2: 326, 1931.

2317. Müller, P., Helvetica chimica acta (Basel) 29: 1560, 1946.

2318. Mullins, L. J., Science 122: 118, 1955.

2319. Muma, H. H., and Hixon, E., The Journal of Economic Entomology 42: 231, 1949.

2320. Munch, J. C., The Journal of the American Medical Association 102: 1929, 1934.

2321. Munch, J. C., "Toxicity of Chlorinated Hydrocarbon Insecticides".

2322. Munch, J. C., and Silver, J., U.S. Department of Agriculture Bulletin No. 238, 1931.

2323. Munro, H. A. U., Department of Agriculture (Canada, Dominion of) Scientific Service Publication No. 655, 1951.

2324. Munro, H. A. U., Scientific Agriculture (Canada, Dominion of) 27: 267, 1947.

2325. Munro, J. A., and Carruth, L. A., The Journal of Economic Entomology 25: 896, 1932.

2326. Munson, S. C., et al., The Journal of Economic Entomology 47: 578, 1954.

2327. Munson, S. C., and Yeager, J. F., Annals of the Entomological Society of America 40: 475, 1947.

2328. Munson, S. C., and Yeager, J. F., The Journal of Economic Entomology 38: 634, 1945.
2329. Murphy, D. F., The Journal of Economic Entomology 29(3): 606, 1936.
2330. Murphy, D. F., and Peet, C. H., Industrial and Engineering Chemistry 25: 638, 1933.
2331. Murphy, D. F., and Peet, C. H., The Journal of Economic Entomology 25(1): 123, 1932.
2332. Murray, D., and Spinks, J., Canadian Journal of Chemistry 30: 497, 1952.
2333. Musgrave, A. J., and Salkeld, E. L., The Canadian Entomologist 82: 177, 1950.
2334. Myburgh, A. C., Journal of the Entomological Society of Southern Africa (Pretoria, Union of South Africa) 8: 162, 1945.
2335. Myers, D., et al., Nature (London) 170: 805, 1952.
2336. Myers, D., and Mendel, Nature (London) 170: 928, 1952.
2337. Mylius, A., and Koechlin, H., Helvetica chimica acta (Basel) 29: 405, 1946.
2338. Nachmansohn, D., et al., The Journal of Biological Chemistry 174: 247, 1948.
2339. Ibid., 180: 875, 1949.
2340. Nachmansohn, D., and Feld, E., The Journal of Biological Chemistry 171: 715, 1947.
2341. Nachmansohn, D., and Rothenberg, M., The Journal of Biological Chemistry 168: 223, 1947.
2342. Nachmansohn, D., and Wilson, I., Advances in Enzymology 12: 259, 1951.
2343. Nagai, K., Journal of the Tokyo Chemical Society (Japan) 23: 744, 1902.
2344. Nash, R., Annals of Applied Biology 41: 652, 1954.
2345. National Academy of Sciences - National Research Council (U. S.), "Safe Handling of Pesticides Employed in Public Health", (mimeograph report), 1954.
2346. Nauck, E. G., F I A T Review of German Science 1939 - 1946 (Wiesbaden).
2347. Neal, P. A., et al., Public Health Reports (Washington, D.C.) 61: 403, 1946.
2348. Ibid., Supplement 177, 1944.
2349. Neal, P. A., et al., Public Health Bulletin, Supplement 183, 1945 (Washington, D.C.)
2350. Neal, P. A., and Von Oettingen, W. F., Soap and Sanitary Chemicals 22(7): 135, 1946.
2351. Negus, S. S., Journal of the American Water Works Association 30: 242, 1938.
2352. Neifert, I. E., et al., U.S. Department of Agriculture Bulletin No. 1313, 1925.
2353. Neiswander, C. R., The Journal of Economic Entomology 28(2): 405, 1935.
2354. Neiswander, C. R., et al., The Journal of Economic Entomology 43: 633, 1950.
2355. Neiswander, C. R., and Morris, V. H., The Journal of Economic Entomology 33(3): 517, 1940.
2356. Neiswander, R. B., The Journal of Economic Entomology 42(1): 41, 1949.
2357. Neiswander, R. B., and Davidson, R. H., The Journal of Economic Entomology 41(4): 652, 1948.
2358. Neiswander, R. B., and Rodriguez, J. G., The Journal of Economic Entomology 40: 419, 1947.
2359. Nelson, A. A., et al., Public Health Reports (Washington, D.C.) 59: 1009, 1944.
2360. Nelson, A. A., and Woodard, G., Archives of Pathology (Chicago) 48: 387, 1949.
2361. Nelson, A. A., and Woodard, G., Federation Proceedings 7: 276, 1948.
2362. Nelson, A. L., and Surber, E. W., U.S. Department of the Interior, Fish and Wildlife Service Special Report No. 41, 1947.
2363. Nelson, E. M., et al., Science 78: 124, 1933.
2364. Nelson, R. H., et al., The Journal of Economic Entomology 42(1): 158, 1949.
2365. Ibid., 43(3): 393, 1950.
2366. Nelson, R. H., et al., Soap and Sanitary Chemicals 25(1): 120, 1949.
2367. Nelson, S. C., et al., Unpublished data contributed by Hamman, R. E., on behalf of Shell Chemical Corporation; Utah Agricultural Experiment Station, 1955.
2368. Newcomer, E. J., American Fruit-Grower 69(2): 18, 1949.
2369. Newcomer, E. J., The Journal of Economic Entomology 41: 691, 1948.
2370. Newcomer, E. J., U.S. Department of Agriculture Technical Bulletin No. 281, 1932.
2371. Newcomer, E. J., and Carter, R. H., U.S. Department of Agriculture Technical Bulletin No. 373, 1933.
2372. Newcomer, E. J., and Dean, F. P., The Journal of Economic Entomology 39: 783, 1946.
2373. Ibid., 41: 691, 1948.
2374. Ibid., 42(5): 857, 1949.
2375. Newhall, A. G., Soil Science 61: 67, 1946.
2376. Newman, J. F., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, Volume II, p. 331.
2377. Newsome, I. E., et al., Journal of the American Veterinary Medical Association 76: 826, 1930.
2378. Newton, H. C. F., et al., Nature (London) 158: 417, 1946.
2379. Newton, J. H., and List, G. M., The Journal of Economic Entomology 42: 346, 1949.
2380. Nichols, J., and Gardner, L. I., The Journal of Laboratory and Clinical Medicine 37: 229, 1951.
2381. Nichols, J., and Green, H. D., The American Journal of Physiology 176: 374, 1954.
2382. Nickels, C. B., The Journal of Economic Entomology 43: 552, 1950.
2383. Nielsen, O. S., and Piper, J., Ugeskrift for laeger (København) 112: 146, 1950.
2384. Noble, N. S., Agricultural Gazette of New South Wales (Australia, Dominion of) 46: 573, 1935.
2385. Nolte, M. C. A., Department of Agriculture and Forestry, South Africa (Union of,) Scientific Bulletin No. 232, 1940.
2386. Norris, M. V., et al., Journal of Agricultural and Food Chemistry 2(11): 570, 1954.
2387. Northern, R. T., Bulletin of the American Orchid Society 20: 531, 1951.
2388. Norton, L. B., The Journal of Economic Entomology 34(1): 80, 1941.
2389. Norton, R., Contributions from the Boyce Thompson Institute 17: 105, 1953.
2390. Nuckolls, A. H., Underwriter's Laboratories Report, Miscellaneous Hazards, No. 2375, 1933.
2391. O'Brien, R. D., The Journal of Economic Entomology 49(4): 484, 1956.
2392. O'Brien, R. D., and Spencer, E. Y., Journal of Agricultural and Food Chemistry 1(15): 946, 1953.
2393. Ibid., 3(1): 56, 1955.
2394. O'Colla, P., Journal of the Science of Food and Agriculture 3: 130, 1952.
2395. O'Dell, Proceedings of the Society for Experimental Biology and Medicine 85: 400, 1954.
2396. Odum, E. P., and Summerford, W. T., Science 104: 480, 1946.
2397. Oelkers, H. A., and Fiedler, H., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 195: 117, 1940.

2398. Oeming, L. F., Sewage Works Journal 18: 678, 1946.

2399. Ofner, R. R., et al., Federation Proceedings 4: 132, 1945.

2400. Ohio River Valley Water Sanitation Commission, Sub-Committee on Toxicities, Report No. 3, 1950.

2401. Ohnesorge, G., Deutsche medizinische Wochenschrift (Leipzig) 56: 961, 1930.

2402. O'Kane, W. C., Industrial and Engineering Chemistry 15: 911, 1923.

2403. O'Kane, W. C., The Journal of Economic Entomology 40(1): 133, 1947.

2404. O'Kane, W. C., et al., New Hampshire Agricultural Experiment Station Bulletin No. 183, 1917.

2405. Ibid., Technical Bulletin No. 54, 1933.

2406. O'Kane, W. C., and Conklin, J. G., New Hampshire Agricultural Experiment Station Technical Bulletin No. 40, 1930.

2407. O'Kane, W. C., and Glover, L. C., New Hampshire Agricultural Experiment Station Technical Bulletin No. 63, 1935.

2408. Ibid., Technical Bulletin No. 65, 1936.

2409. O'Kane, W. C., and Smith, H. W., The Journal of Economic Entomology 34: 438, 1941.

2410. Okinaka, J., The Journal of Pharmacology and Experimental Therapeutics 112: 231, 1954.

2411. Oliver, A. D., and Eden, W. G., The Journal of Economic Entomology 48(1): 111, 1955.

2412. Onaka, M., Zeitschrift für physiologische Chemie (Hoppe-Seylers), Leipzig 70: 433, 1911; 71: 193, 1911.

2413. Oosterhuis, A. G., and Wibaut, J. P., Recueil des travaux chimiques des Pays - Bas (et de la Belgique) (Amsterdam; The Hague) 55: 729, 1936.

2414. Oosthuizen, M. J., Journal of the Entomological Society of Southern Africa (Pretoria) 7: 100, 1944.

2415. Oppenoorth, F., Nature (London) 173: 1000, 1954.

2416. Orde, and Thompson, Biochemical Journal (London) 51: 245, 1952.

2417. Orekhov, A., Journal of General Chemistry (U.S.S.R.) 7: 2048, 1937.

2418. Orekhov, A., and Menschikov, G., Berichte; Deutsche chemische Gesellschaft (Berlin) B64: 266, 1931; B65: 232, 1932.

2419. Orekhov, A., and Menschikov, G., Comptes rendus hebdomadaires des séances de l'Académie des sciences (Paris) 189: 945, 1929.

2420. Orr, L. W., and Mott, L. O., The Journal of Economic Entomology 38: 428, 1945.

2421. Orser, W. B., and Brown, A. W. A., Canadian Journal of Zoology 29: 54, 1951.

2422. Osburn, M. R., Florida Entomologist 31: 11, 1948.

2423. Osburn, M. R., The Journal of Economic Entomology 42: 542, 1949.

2424. Osburn, M. R., and Lipp, J. W., U.S. Department of Agriculture Circular No. 373, 1935.

2425. Ossowski, L. L., Endeavour (London) 3: 32, 1944.

2426. Oxley, T., Journal of the Indian Archipelago and East Asia 2(10): 641, 1848.

2427. Packard, C. M., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.

2428. Packard, C. M., The Journal of Economic Entomology 39: 669, 1946.

2429. Pagan, C., and Hageman, R. H., Science 112: 222, 1950.

2430. Page, A. B. P., et al., Journal of the Society of Chemical Industry (London) 68: 102; 151, 1949.

2431. Page, A. B. P., et al., Annals of Applied Biology 36: 225, 1949.

2432. Page, A. B. P., and Blacklith, R. E., Annals of Applied Biology 36: 244, 1949.

2433. Painter, E. P., Chemical Reviews 28: 179, 1941.

2434. Pal, R., and Sharma, M. I. D., Transactions of the IXth International Congress of Entomology, Amsterdam 1951, Volume II, p. 346.

2435. Panas, M., Comptes Rendus hebdomadaires des séances de l'Académie des sciences (Paris) 107: 921, 1888.

2436. Panhoff, Archiv für Anatomie und Physiologie p. 419, 1881.

2437. Pankaskie, J. E., et al., The Journal of Economic Entomology 45(1): 51, 1952.

2438. Parencia, C. R., and Ewing, K. P., The Journal of Economic Entomology 41: 735, 1948.

2439. Parfentjev, J. A., Transactions of the IVth International Congress of Entomology, Ithaca, New York 1928, Volume II, p. 857.

2440. Parfentjev, J. A., and Devrient, W., Biochemische Zeitschrift (Berlin) 217: 368, 1930.

2441. Parish, H. E., and Knipling, E. F., The Journal of Economic Entomology 35(1): 70, 1942.

2442. Park, W. E., Minnesota Medicine (Minneapolis) 33: 360, 1950.

2443. Parker, British Journal of Industrial Medicine 8: 226, 1951.

2444. Parker, J. R., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.

2445. Parker, J. R., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine No. E-807, 1950.

2446. Parker, J. R., et al., U.S. Department of Agriculture Bulletin No. EC-7, 1949.

2447. Parker, J. R., and Schweis, G. G., The Journal of Economic Entomology 37(2): 309, 1944.

2448. Parker, R. L., and Eshbaugh, E. L., The Journal of Economic Entomology 40: 861, 1947.

2449. Parker, V., Biochemical Journal (London) 51: 363, 1952.

2450. Parker, W. L., et al., The Journal of Economic Entomology 41(2): 275, 1948.

2451. Parker, W. L., and Beacher, J. H., Delaware Agricultural Experiment Station Bulletin No. 264, 1947.

2452. Parkin, E. A., Annals of Applied Biology 33: 97, 1946.

2453. Parkin, E. A., Annual Review of Entomology 1: 223, 1956.

2454. Parkin, E. A., and Green, A. A., Nature (London) 154: 16, 1944.

2455. Parmenter, D. C., The Journal of Industrial Hygiene and Toxicology 2: 456, 1920/1921.

2456. Parrott, P. J., et al., New York State Agricultural Experiment Station Bulletin No. 262, 1905.

2457. Pasfield, G., Agricultural Gazette of New South Wales (Australia, Dominion of) 56: 489, 1945.

2458. Pasquier, R., France. Office National Anti-Acridien. Bulletin Semestriel, Algérie 4: 5, 1947.

2459. Patton, R. L., Journal of Agricultural Research (Washington, D.C.) 67: 411, 1943.

2460. Pearce, C. W., et al., Journal of the American Chemical Society 58: 1104, 1936.

2461. Ibid., 59: 1258, 1937.

2462. Pearce, C. W., et al., Science 116: 254, 1952.
2463. Pearson, A. M., and Richardson, C. H., The Journal of Economic Entomology 26: 486, 1933.
2464. Peck, D., Chemistry and Industry, 1948, p. 526.
2465. Pederson, C. E., and Sherman, F., The Journal of Economic Entomology 41: 659, 1948.
2466. Peffly, R. L., and Gahan, J. B., The Journal of Economic Entomology 42: 113, 1949.
2467. Pellegrini, J., et al., The Journal of Economic Entomology 45(3): 532, 1952.
2468. Pendse, G. S., et al., Current Science (Bangalore, India) 14: 37, 1945.
2469. Pendse, G. S., et al., Journal of the University of Bombay (India) 15A: (New Series Part 3, No. 20) 26, 1946.
2470. Pepper, B. B., et al., The Journal of Economic Entomology 40: 727, 1947.
2471. Pepper, J., and Hastings, E., The Journal of Economic Entomology 36: 633, 1943.
2472. Perron, Y., and Barre, R., Canadian Journal of Chemistry 30: 203, 1952.
2473. Perry, A. S., et al., The Biological Bulletin 104: 426, 1953.
2474. Perry, A. S., et al., Journal of Agricultural and Food Chemistry 3(12): 1008, 1955.
2475. Perry, A. S., et al., The Journal of Economic Entomology 46: 972, 1953.
2476. Perry, A. S., and Hoskins, W. M., The Journal of Economic Entomology 44: 839, 1951.
2477. Ibid., 44: 850, 1951.
2478. Perry, A. S., and Hoskins, W. M., Science 111: 600, 1950.
2479. Perucci, E., Tobacco (London) 56: 362, 1952.
2480. Pest Control, Limited, Chemistry and Industry, 1951, p. 123.
2481. Petch, C. E., Department of Agriculture of Canada (Dominion of), Division of Entomology Publication No. 57, 1946.
2482. Peters, B. D., and Fenwick, D. W., Annals of Applied Biology 36: 364, 1949.
2483. Peters, G., Anzeiger für Schädlingskunde (Berlin) 14: 116, 1938.
2484. Peters, G., "Chemie und Toxikologie der Schädlingsbekämpfung", Samml. Chem. u. Chem.-Tech. Vorträge N.F., F. Enke Verlag, Stuttgart, 1936.
2485. Peters, G., Chemiker-Zeitung 63: 41, 1939.
2486. Ibid., 64: 485, 1940.
2487. Peters, G., and Ganter, W., Zeitschrift für angewandte Entomologie (Berlin) 21: 547, 1935.
2488. Peters, L., Proceedings of the Society for Experimental Biology and Medicine 72: 304, 1949.
2489. Peters, R. A., et al., Nature (London) 156: 616, 1945.
2490. Peterson, A., The Journal of Economic Entomology 10: 556, 1917.
2491. Peterson, A., The Ohio Journal of Science (Columbus) 46: 323, 1946.
2492. Petty, B. K., Department of Agriculture and Forestry, South Africa (Union of), Scientific Bulletin No. 276, 1946.
2493. Petry, Zentralblatt für Arbeitsmedizin und Arbeitsschutz 1: 86, 1951.
2494. Pettey, F. W., Department of Agriculture and Forestry, South Africa (Union of), Entomological Memoirs 2: 33, 1924.
2495. Pfeiffer, C. C., et al., The Journal of the American Medical Association 128: 266, 1945.
2496. Pflesser, G., Archiv für Gewerbepathologie und Gewerbehygiene (Berlin) 8: 591, 1938.
2497. Philips, F. S., and Gilman, A., The Journal of Pharmacology and Experimental Therapeutics 86: 213, 1946.
2498. Phillipot, E., and Dallemagne, M. J., Experientia (Basel) 3: 118, 1947.
2499. Phillips, C. R., and Kayser, S., The American Journal of Hygiene 50: 270, 1949.
2500. Phillips, G. L., and Bodenstein, W. G., The Journal of Economic Entomology 41: 804, 1948.
2501. Phillips, W. R., and Munro, H. A. U., The Journal of Economic Entomology 32: 344, 1939.
2502. Picard, J., and Kearns, C. W., Canadian Journal of Research 27: 31, 1949.
2503. Pickles, A., Review of Applied Entomology (London) A37: 83, 1949.
2504. Pictet, A., and Rotschy, A., Berichte; Deutsche chemische Gesellschaft (Berlin) 37: 1225, 1904.
2505. Pielou, D. P., Nature (London) 158: 378, 1946.
2506. Pierpont, R. L., University of Delaware Agricultural Experiment Station Technical Bulletin No. 253, 1945.
2507. Pietri-Tonelli(de), P., and March, R. B., The Journal of Economic Entomology 47(5): 902, 1954.
2508. Pijoan, M., Soap and Sanitary Chemicals 23: 124; 173; 175, 1947.
2509. Pijoan, M., et al., United States Naval Medical Bulletin (Washington D.C.) 46: 1506, 1946.
2510. Pilat, M., Bulletin of Entomological Research (London) 26: 165, 1935.
2511. Ibid., 26: 283, 1935.
2512. Pimentel, D., et al., Annals of the Entomological Society of America 47: 208, 1954.
2513. Piquett, P. G., et al., The Journal of Economic Entomology 40(4): 577, 1947.
2514. Pirie, H., Chemistry and Industry 1951, February 10.
2515. Plackett, R., and Hewlett, P., Annals of Applied Biology 35: 347, 1948.
2516. Plank, H. K., Puerto Rico Federal Experiment Station (Mayaguez) Bulletin No. 49, 1950.
2517. Plummer, C. C., and Shaw, J. G., The Journal of Economic Entomology 42: 708, 1949.
2518. Pluvinage, R. J., and Heath, J. W., Proceedings of the Society for Experimental Biology and Medicine 63: 212, 1946.
2519. Polivka, J. B., The Journal of Economic Entomology 43(3): 391, 1950.
2520. Pollock, G. H., and Wang, R. I. H., Science 117: 596, 1953.
2521. Pollock, R. W., Northwest Medicine (Seattle) 52: 293, 1953.
2522. Polonovski, M., and Polonovski, M., Comptes rendus hebdomadaires des séances de l'Académie des sciences (Paris) 184: 1333, 1927.
2523. Popenoe, C. H., Science 64: 525, 1926.
2524. Porter, B. A., American Fruit Grower 68(2): 19, 1948.
2525. Porter, B. A., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D. C.
2526. Porter, B. H., and Fahey, J. E., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
2527. Portier, P., Comptes rendus des séances de la Société de biologie (Paris) 105: 367, 1930/1931.
2528. Portman, R. W., The Journal of Economic Entomology 40(1): 134, 1947.
2529. Pospelov, V. P., et al., Biological Abstracts 4: item No. 12519.

2530. Post, R. L., et al., North Dakota Agricultural Experiment Station Bi-Monthly Bulletin 10: 26, 1948.

2531. Potter, C., Annals of Applied Biology 28: 142, 1941.

2532. Potter, C., and Gillham, E. M., Annals of Applied Biology 33(2): 142, 1946.

2533. Potter, C., and Musgrave, A. J., Annals of Applied Biology 27: 110, 1940.

2534. Potts, S. F., The Journal of Economic Entomology 39(6): 716, 1946.

2535. Potts, W., and Vanderplanck, F., Nature (London) 156: 112, 1945.

2536. Pradhan, S., Bulletin of Entomological Research (London) 40: 239, 1949.

2537. Pratt, F. S., et al., The Journal of Economic Entomology 26: 1031, 1933.

2538. Pratt, J. J., and Babers, F. H., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C., p. 205.

2539. Pratt, J. J., and Babers, F. H., The Journal of Economic Entomology 46: 864, 1953.

2540. Prell, H., Kranke Pflanze 2: 242, 1925.

2541. Price, W. A., Indiana Agricultural Experiment Station Bulletin No. 247, 1920.

2542. Prill, E. A., et al., Contributions from the Boyce Thompson Institute 14: 127, 1946.

2543. Ibid., 14: 341, 1946.

2544. Ibid., 14: 397, 1947.

2545. Prill, E. A., et al., Science 101: 464, 1945.

2546. Prill, E. A., and Synerholm, M. E., Contributions from the Boyce Thompson Institute 14: 221, 1946.

2547. Princi, F., World Crops, August, 1954. (Reprint)

2548. Princi, F., and Spurbeck, G. H., Archives of Industrial Hygiene and Occupational Medicine 3: 64, 1951.

2549. Pritchard, A. E., California Agriculture May, 1951, p. 9.

2550. Pritchard, A. E., and Beer, R. E., The Journal of Economic Entomology 42: 372, 1949.

2551. Proverbs, M., and Morrison, F. O., Canadian Journal of Research 25: 12, 1947.

2552. Pulver, R., and Domenjoz, R., Experientia (Basel) 7: 306, 1951.

2553. Punt, A., Acta brevia Neerlandica de physiologia, pharmacologia, microbiologia e. a. (Amsterdam) 14: 76, 1946.

2554. Pussard, R., Comptes rendus hebdomadaires des séances de l'Académie d'Agriculture de France, Ministère d'Agriculture 32: 695, 1946.

2555. Putnam, L. G., Department of Agriculture, Canada (Dominion of), Division of Entomology Publication No. 73, 1949.

2556. Pyenson, L., and MacLeod, G. F., Journal of Agricultural Research (Washington, D.C.) 52(9): 705, 1936.

2557. Quaintance, A. L., and Siegler, E. H., U. S. Department of Agriculture Farmer's Bulletin No. 1666, 1931.

2558. Quarterman, K. D., Communicable Disease Center Bulletin (U. S. Public Health Service, Savannah, Georgia) 9(11): 3, 1950.

2559. Quayle, H. J., University of California Journal of Agriculture 3: 333, 1916.

2560. Quayle, H. J., Hilgardia 11: 183, 1938.

2561. Quayle, H. J., The Journal of Economic Entomology 16: 327, 1923.

2562. Ibid., 36: 493, 1943.

2563. Questel, D. D., et al., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine Bulletin No. E-557, 1941.

2564. Questel, D. D., and Connin, R. V., The Journal of Economic Entomology 40(6): 914, 1947.

2565. Questel, D. D., and Connin, R. V., U. S. Department of Agriculture, Bureau of Entomology and Plant Quarantine Bulletin No. E-785, 1949.

2566. Questel, D. D., and Gertler, S. I., U. S. Department of Agriculture, Bureau of Entomology and Plant Quarantine Circular No. E-707, 1946.

2567. Radeleff, R. D., Contributed Data, 1954.

2568. Radeleff, R. D., Veterinary Medicine (Chicago) 43: 342, 1948.

2569. Ibid., 44: 436, 1949.

2570. Ibid., 49(1): 15, 1954.

2571. Radeleff, R. D., et al., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.

2572. Radeleff, R. D., et al., Veterinary Medicine (Chicago) 46: 305, 1951.

2573. Radeleff, R. D., and Bushland, R. C., The Journal of Economic Entomology 43(3): 358, 1950.

2574. Raffy, A., and Portier, P., Comptes rendus des séances de la Société de biologie (Paris) 108: 1062, 1931.

2575. Rai, L., et al., The Journal of Economic Entomology 49(3): 307, 1956.

2576. Rai, L., and Roan, C. C., The Journal of Economic Entomology 49(5): 591, 1956.

2577. Rainwater, C. F., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.

2578. Rainwater, C. F., The Journal of Economic Entomology 40: 923, 1947.

2579. Ramsey, L., and Patterson, W., Journal of the Association of Official Agricultural Chemists 29: 337, 1946.

2580. Raucourt, M., Revue technique de la protection des végétaux (Paris) 1(2): 169, 1947.

2581. Raun, E. S., The Journal of Economic Entomology 49(5): 628, 1956.

2582. Raun, E. S., and Ahrens, R. H., The Journal of Economic Entomology 49(1): 140, 1956.

2583. Rawlins, W. A., et al., The Journal of Economic Entomology 42(2): 326, 1949.

2584. Rawlins, W. A., and Newhall, A., The Journal of Economic Entomology 43(6): 950, 1950.

2585. Rea, J. M., et al., The Journal of Economic Entomology 47(1): 48, 1954.

2586. Read, W. H., Nursery and Market Garden Industry Development Society, Limited, Experiment and Research Stations Annual Report 13: 69, 1927.

2587. Read, W. H., Report of the Experimental Research Station at Cheshunt (Great Britain), 1945, p. 57.

2588. Ibid., 1949, p. 57.

2589. Read, W. H., and Smith, H. J., Report of the Experimental Research Station at Cheshunt (Great Britain), 1950.

2590. Reed, J. P., and Filmer, R. S., The Journal of Economic Entomology 43(1): 161, 1950.

2591. Reed, W. D., and Harrison, P, K., The Journal of Economic Entomology 33(5): 812, 1940.

2592. Reed, W. D., and Livingstone, E. M., The Journal of Economic Entomology 31(1): 125, 1938.

2593. Reeves, G. I., The Journal of Economic Entomology 18: 83, 1925.

2594. Reuss, Dissertation, Universität zu Würzburg 1931.

2595. Reynolds, H. T., et al., The Journal of Economic Entomology 46(4): 555, 1953.

2596. Richards, A. G., Journal of the New York Entomological Society 51: 55, 1943.

2597. Richards, A. G., Transactions of the Entomological Society of America 67: 161, 1941.

2598. Richards, A. G., and Cutkomp, L. K., The Biological Bulletin 90: 97, 1946.
2599. Richards, A. G., and Cutkomp, L. K., The Journal of Cellular and Comparative Physiology 26: 57, 1945.
2600. Richards, A. G., and Cutkomp, L. K., Journal of the New York Entomological Society 53: 313, 1945.
2601. Richards, A. G., and Weygandt, J. L., Journal of the New York Entomological Society 53: 153, 1945.
2602. Richardson, B. H., and Wene, G. P., The Journal of Economic Entomology 49(3): 333, 1956.
2603. Richardson, C. H., The Journal of Economic Entomology 38(4): 478, 1945.
2604. Ibid., 38(6): 710, 1945.
2605. Ibid., 39(5): 598, 1946.
2606. Richardson, C. H., et al., The Journal of Economic Entomology 29(5): 850, 1936.
2607. Richardson, C. H., et al., Science 80: 76, 1934.
2608. Richardson, C. H., and Haas, L. E., Iowa State College Journal of Science 6: 287, 1932.
2609. Richardson, C. H., and Haas, L. E., The Journal of Economic Entomology 24: 732, 1931.
2610. Ibid., 25: 1078, 1932.
2611. Richardson, C. H., and Seiferle, E. J., The Journal of Economic Entomology 32(2): 297, 1939.
2612. Ibid., 33(6): 857, 1940.
2613. Richardson, C. H., and Shepard, H. H., Journal of Agricultural Research (Washington, D.C.) 40: 1007, 1930.
2614. Ibid., 41: 337, 1930.
2615. Richardson, C. H., and Smith, C. R., Journal of Agricultural Research (Washington, D.C.) 33: 597, 1926.
2616. Richardson, C. H., and Smith, C. R., U.S. Department of Agriculture Bulletin No. 1160, 1926.
2617. Richardson, C. H., and Thurber, G. A., The Journal of Economic Entomology 26: 494, 1933.
2618. Richardson, C. H., and Walkden, H. H., The Journal of Economic Entomology 38(4): 471, 1945.
2619. Richardson, H. H., The Journal of Economic Entomology 24: 763, 1931.
2620. Ibid., 28(2): 399, 1935.
2621. Ibid., 33(2): 368, 1940.
2622. Ibid., 36(3): 420, 1943.
2623. Ibid., 38(4): 478, 1945.
2624. Richardson, H. H., U.S. Department of Agriculture Technical Bulletin No. 853, 1943.
2625. Richardson, H. H., et al., The Journal of Economic Entomology 36(1): 111, 1943.
2626. Ibid., 37(1): 111, 1944.
2627. Richardson, H. H., and Busbey, R. L., The Journal of Economic Entomology 30: 576, 1937.
2628. Richardson, H. H., and Casanges, A. H., The Journal of Economic Entomology 35(2): 242, 1942.
2629. Ibid., 35(5): 664, 1942.
2630. Ibid., 36(4): 420, 1943.
2631. Richardson, H. H., and Roth, H., The Journal of Economic Entomology 49(5): 715, 1956.
2632. Richardson, H. H., and Schecter, M. S., The Journal of Economic Entomology 36(1): 110, 1943.
2633. Richter, P. O., The Journal of Economic Entomology 34(1): 67, 1941.
2634. Richter, P. O., and Jewett, H. H., The Journal of Economic Entomology 35(3): 441, 1942.
2635. Riedeburg, T., Agricultural Chemicals 7(4): 52, 1952.
2636. Rieman, E. H., Soap and Sanitary Chemicals 22(10): 135, 1946.
2637. Riemschneider, R., Angewandte Chemie 61: 333, 1949.
2638. Riemschneider, R., Euclides (Madrid) 12: 35, 1952.
2639. Riemschneider, R., Die Pharmazie (Berlin) 9(1): 1950.
2640. Riemschneider, R., Chimie et industrie 64: 695, 1950.
2641. Riemschneider, R., Journal of the American Chemical Society 73: 1374, 1951.
2642. Riemschneider, R., Monatshefte für Chemie und Verwandte Teile anderen Wissenschaften 82: 600, 1951.
2643. Riemschneider, R., Zeitschrift für Naturforschung (Wiesbaden) 6b: 395, 1951.
2644. Ibid., 7b: 277, 1952.
2645. Riemschneider, R., and Kluge, A., Zeitschrift für Naturforschung (Wiesbaden) 8b: 696, 1953.
2646. Riker, W. F., Pharmacological Reviews (Baltimore) 5: 1, 1953.
2647. Riker, W. F., et al., The Journal of Pharmacology and Experimental Therapeutics 88: 327, 1946.
2648. Ripley, L. B., et al., Department of Agriculture, South Africa (Union of), Scientific Bulletin No. 259, 1947.
2649. Ripley, L. B., and Hepburn, G. A., Department of Agriculture, South Africa (Union of), Entomological Memoirs 7: 17, 1931.
2650. Ripper, W. E., Annual Review of Entomology 1: 403, 1956.
2651. Ripper, W. E., Compte Rendu; IIIme Congrès international de phytopharmacie, Paris 1952, p. 171.
2652. Ripper, W. E., Nature (London) 153: 448, 1944.
2653. Ripper, W. E., et al., Bulletin of Entomological Research (London) 40: 681, 1950.
2654. Ripper, W. E., et al., The Journal of Economic Entomology 44(3): 448, 1951.
2655. Ripper, W. E., et al., Nature (London) 163: 787, 1949.
2656. Ritlop, Zeitschrift für die gesamte experimentelle Medizin (Berlin) 106: 296, 1939.
2657. Roan, C., et al., The Journal of Economic Entomology 43: 319, 1950.
2658. Roan, C., and Maeda, S., The Journal of Economic Entomology 46: 775, 1953.
2659. Ibid., 47(3): 507, 1954.
2660. Roark, R. C., Agricultural Chemicals 1(3): 21, 1946.
2661. Ibid., 1(4): 29, 1946.
2662. Roark, R. C., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
2663. Roark, R. C., The Journal of Economic Entomology 34: 684, 1941.
2664. Roark, R. C., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine No. E-537, 1941.
2665. Ibid., No. E-639, 1945.
2666. Ibid., No. E-802, 1950.
2667. Ibid., No. E-846, 1952.
2668. Roark, R. C., U.S. Department of Agriculture, Miscellaneous Publication No. 176.
2669. Roark, R. C., and Busbey, R. L., U.S. Department of Agriculture, Circular No. E-351, 1935.
2670. Roark, R. C., and Cotton, R. T., U.S. Department of Agriculture, Technical Bulletin No. 162, 1929.
2671. Roark, R. C., and Nelson, O. A., The Journal of Economic Entomology 22: 381, 1929.
2672. Robbins, C. S., et al., Journal of Wildlife Management 15: 213, 1951.

2673. Robbins, C. S., and Stewart, R. E., Journal of Wildlife Management 13: 11, 1949.
2674. Robbins, W. E., et al., The Journal of Economic Entomology 49(6): 801, 1956.
2675. Robbins, W. E., and Dahm, P. A., Journal of Agricultural and Food Chemistry 3(6): 500, 1955.
2676. Robbins, W. W., et al., "Weed Control", McGraw-Hill, New York, 1942.
2677. Robertson, O. T., The Journal of Economic Entomology 41(1): 120, 1948.
2678. Robinson, G., Bulletin of Entomological Research (London) 33: 273, 1942.
2679. Robinson, G., Parasitology (London) 34: 113, 1942.
2680. Rodriguez, Archives de la Sociedad de biología de Montevideo 18: 46, 1951.
2681. Roeder, K. D., Armed Services Research Division (U.S.) Report No. 1, (Insect and Rodent Control), 1948.
2682. Roeder, K. D., Bulletin of the Johns Hopkins Hospital (Baltimore) 83: 587, 1948.
2683. Roeder, K. D., et al., Journal of Neurophysiology 10: 1, 1947.
2684. Roeder, K. D., and Kennedy, N. K., Federation Proceedings 6(1): 1947.
2685. Roeder, K. D., and Roeder, S., The Journal of Cellular and Comparative Physiology 14: 1, 1939.
2686. Roeder, K. D., and Weiant, E., Annals of the Entomological Society of America 44: 372, 1951.
2687. Roeder, K. D., and Weiant, E., The Journal of Cellular and Comparative Physiology 32: 175, 1948.
2688. Roeder, K. D., and Weiant, E., Science 103: 304, 1946.
2689. Rogers, E. F., et al., Journal of the American Chemical Society 70: 3086, 1948.
2690. Ibid., 75: 2991, 1953.
2691. Rogoff, W. M., The Journal of Economic Entomology 45: 1065, 1952.
2692. Rogoff, W. M., and Metcalf, R. L., The Journal of Economic Entomology 44(6): 910, 1951.
2693. Rohm and Haas, Announcement in Agricultural Chemicals 8(6): 47, 1953.
2694. Rohm and Haas, U. S. Patent No. 2,220,521.
2695. Roholm, Heffters Handbuch der experimentelle Pharmakologie E.7: 27.
2696. Rohrbaugh, P. W., The Journal of Economic Entomology 34: 812, 1941.
2697. Rohrbaugh, P. W., Plant Physiology 9: 699, 1941.
2698. Rohwer, S. A., Agricultural Chemicals 4(8): 75, 1949.
2699. Rohwer, S. F., et al., The Journal of the American Medical Association 144(2): 104, 1950.
2700. Rosenfels, R. S., and Crafts, A. S., Hilgardia 12: 203, 1939.
2701. Rosenheim, A., et al., Berichte; Deutsche chemische Gesellschaft (Berlin) 39: 2837, 1906.
2702. Rosenheim, A., and Pritze, M., Berichte; Deutsche chemische Gesellschaft (Berlin) 41: 2708, 1908.
2703. Rosenstiel, R. G., The Journal of Economic Entomology 36: 800, 1943.
2704. Ibid., 42(1): 37, 1949.
2705. Ross, W. A., General Report of the 5th Commonwealth Entomological Congress, London 1948.
2706. Ross, W. A., and Armstrong, T., Scientific Agriculture (Canada) 29: 81, 1949.
2707. Roth, A. R., The Journal of Economic Entomology 47(2): 361, 1954.
2708. Roth, A. R., et al., The Journal of Economic Entomology 46(1): 127, 1953.
2709. Rotman, M. N., et al., Review of Applied Entomology (London) A25: 799, 1936.
2710. Rowe, V. K., et al., Archives of Industrial Hygiene and Occupational Medicine 5: 566, 1952.
2711. Ibid., 6: 158, 1952.
2712. Rowe, V. K., et al., Journal of Agricultural and Food Chemistry 2: 13, 1954.
2713. Roy, D., et al., Annals of Applied Biology 30: 42, 1943.
2714. Rubow, Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 52: 173, 1905.
2715. Rude, C. S., The Journal of Economic Entomology 40: 301, 1947.
2716. Rudolfs, W., et al., Sewage and Industrial Wastes 22: 1157, 1950.
2717. Ibid., 24: 541, 1952.
2718. Rudolfs, W., et al., Sewage Works Journal 16: 222, 1944.
2719. Rueggeberg, W., and Torrance, D., Industrial and Engineering Chemistry 38: 211, 1946.
2720. Ruffin, W. A., and Arant, F. S., Alabama Polytechnic Institute (Auburn), Extension Service Circular No. 376, 1950 (revised).
2721. Russell, F. C., Imperial Bureau of Animal Nutrition (Aberdeen, Scotland) Technical Communication No. 15, 1944.
2722. Ruthruff, R., et al., U.S. Patent No. 2,430,586 (1947).
2723. Sacca, G., Rivista di Parassitologia (Roma) 8: 127, 1947.
2724. Sacktor, B., The Journal of Economic Entomology 43: 832, 1950.
2725. Safro, V. I., The Journal of Economic Entomology 20: 261, 1927.
2726. Sakimura, K., The Journal of Economic Entomology 41(4): 665, 1948.
2727. Salerno, P. R., and Coon, J. M., Archives internationales de pharmacodynamie et de thérapie (Paris) 84: 227, 1950.
2728. Salerno, P. R., and Coon, J. M., The Journal of Pharmacology and Experimental Therapeutics 95: 240, 1949.
2729. Salkeld, E. M., The Canadian Entomologist 83: 39, 1951.
2730. Salkeld, E. M., and Potter, C., Bulletin of Entomological Research (London) 44: 527, 1953.
2731. Salle, J., Archives internationales de pharmacodynamie et de thérapie 82: 181, 1950.
2732. Salle, J., Revue vétérinaire militaire (Paris) 2: 145, 1950.
2733. Sampson, W. W., The Journal of Economic Entomology 49(1): 74, 1956.
2734. Sandground, J. H., The Journal of the American Medical Association 117: 440, 1941.
2735. Santesson, Skandinavisches Archiv für Physiologie 15: 259, 1904.
2736. Sarkaria, D., and Patton, R., Transactions of the American Entomological Society 75: 71, 1949.
2737. Sarles, M. P., and Vandergrift, W. B., The American Journal of Tropical Medicine 29: 151, 1949.
2738. Sarles, M. P., and Vandergrift, W. B., The American Journal of Tropical Medicine and Hygiene 1: 862, 1952.
2739. Sarett, H. P., and Jandorf, B. P., The Journal of Pharmacology and Experimental Therapeutics 91: 339, 1947.
2740. Sass, J. E., Science 114: 466, 1951.
2741. Saunders, J. P., et al., Journal of Agricultural and Food Chemistry 3(9): 762, 1955.

2742. Sautet, J., et al., Comptes rendus hebdomadaires des séances de l'Académie des sciences (Paris) 224: 66, 1947.

2743. Savage, F. E., American Fruit-Grower 68(2): 23, 1948.

2744. Savit, J. J., et al., Proceedings of the Society for Experimental Biology and Medicine 62: 44, 1946.

2745. Sawyer, Science 101: 385, 1945.

2746. Sayers, R. R., et al., Public Health Bulletin (Washington, D.C.) No. 185, 1929.

2747. Sayers, R. R., et al., Public Health Reports (Washington, D.C.) 45: 225, 1930.

2748. Scales, A. L., et al., The Journal of Economic Entomology 43(4): 560, 1950.

2749. Schafer, G. D., Michigan Agricultural Experiment Station Technical Bulletin No. 11, 1911.

2750. Ibid., Technical Bulletin No. 21, 1915.

2751. Schaut, G. G., Journal of the American Water Works Association 31: 771, 1939.

2752. Schechter, M. S., et al., Journal of the American Chemical Society 71: 1517; 3165, 1949.

2753. Ibid., 73: 3541, 1951.

2754. Ibid., 74: 4902, 1952.

2755. Schechter, M. S., and Haller, H. L., The Journal of Organic Chemistry (Baltimore) 8: 194, 1943.

2756. Scherbatscheff, D., Archiv für experimentelle Pathologie und Pharmakologie 47: 1, 1902.

2757. Schibler, W., Schweizerische medizinische Wochenschrift (Basel) 10: 1079, 1929.

2758. Schiemann, O., Zeitschrift für Hygiene und Infektionskrankheiten (Berlin) 78: 389, 1918.

2759. Schifferli, E., Revue médicale de la Suisse romande (Lausanne) 62: 244, 1942.

2760. Schlesinger, E. R., et al., American Journal of Public Health 40: 725, 1950.

2761. Schlingman, A. S., and Gruhzit, O. M., Journal of the American Veterinary Medical Association 71: 187, 1927.

2762. Schlottke, E., Zeitschrift für vergleichende Physiologie (Berlin) 24: 422, 1937.

2763. Schlupp, W. F., Journal of the Department of Agriculture of South Africa (Union of) 4: 132, 1916.

2764. Schmidt, C. H., and Dahm, P. A., The Journal of Economic Entomology 49(6): 729, 1956.

2765. Schmitz, W. R., and Goette, M. B., Soap and Sanitary Chemicals 24(1): 118, 1948.

2766. Schneller, G., and Smith, G., Industrial and Engineering Chemistry 41: 1027, 1949.

2767. Schnitzer, Canadian Public Health Journal (Toronto) 33: 17, 1942.

2768. Schrader, G., Angewandte Chemie 66: 265, 1954.

2769. Schrader, G., British Intelligence Objectives Sub-Committee Report No. 714, 1947. (London, Her Majesty's Stationery Office).

2770. Ibid., Report No. 1095, 1947.

2771. Ibid., Report No. 1808, 1949.

2772. Schrader, G., Höfchen-Briefe für Wissenschaft und Praxis (Bayer Pflanzenschutz Nachrichten) 5(4): 161, 1952.

2773. Schrader, G., "Die Entwicklung neuer Insektizide auf Grundlage organischer Fluor- und Phosphor- Verbindungen", 2 erweiterte Auflage Monographien zu "Angewandte Chemie" und "Chemie - Ingenieur - Technik" No. 62, 1952 (Verlag Chemie G.M.B.H., Weinheim, Deutschland).

2774. Schrader, G., German Patent No. 664,062.

2775. Schrader, G., German Patent No. 720,577 (1942); U.S. Patent No. 2,336,302 (1943).

2776. Schread, J. C., The Journal of Economic Entomology 41: 318, 1948.

2777. Ibid., 41: 905, 1948.

2778. Ibid., 42: 383, 1949.

2779. Ibid., 42: 499, 1949.

2780. Schrenk, H. H., et al., Public Health Reports (Washington, D.C.) 48: 1389, 1933.

2781. Ibid., 51: 1329, 1936.

2782. Schroeder, H. O., et al., The Journal of Economic Entomology 41(6): 890, 1948.

2783. Schulman, S., et al., The Journal of the American Medical Association 152: 1707, 1953.

2784. Schulz, Dissertation, Hamburg, 1936.

2785. Schulz, E. R., and Thompson, N. F., U.S. Department of Agriculture Bulletin No. 1316, 1925.

2786. Schulze, E., Berliner Klinische Wochenschrift 57: 941, 1920.

2787. Schulze, F., et al., The Journal of Economic Entomology 45(6): 1094, 1952.

2788. Schwander, P., Archiv für Gewerbepathologie und Gewerbehygiene (Berlin) 7: 109, 1936.

2789. Schwardt, H. H., The Journal of Economic Entomology 42(3): 444, 1949.

2790. Schwardt, H. H., et al., The Journal of Economic Entomology 40: 363, 1947.

2791. Schwartze, E., The Journal of Pharmacology and Experimental Therapeutics 20: 181, 1922.

2792. Schwitgebel, R. B., Soap and Sanitary Chemicals 22(5): 131, 1946.

2793. Scofield, C. S., and Wilcox, L. V., U.S. Department of Agriculture Technical Bulletin No. 264, 1931.

2794. Scott, D. B., The Journal of Economic Entomology 42: 782, 1949.

2795. Scott, D. B., and Karr, E. H., The Journal of Economic Entomology 35: 702, 1942.

2796. Scott, L. B., The Journal of Economic Entomology 38: 464, 1945.

2797. Scott, L. B., and Milam, J., The Journal of Economic Entomology 36: 335, 1943.

2798. Ibid., 37: 845, 1944.

2799. Sealey, Organic Phosphate Study, Environmental Research Laboratory, University of Washington (State of), December 1951.

2800. Sedoon, H. R., and Ramsay, A. A., Department of Agriculture of New South Wales (Australia), Veterinary Research Report No. 6 (part III) p. 113, 1931.

2801. Seiferle, E., et al., The Journal of Economic Entomology 35: 35, 1942.

2802. Shaffer, C. B., Data and descriptive material on Malathion contributed on behalf of the American Cyanamid Company.

2803. Shaffer, C. B., Data contributed in May, 1955 on behalf of the American Cyanamid Company.

2804. Shanahan, G. J., and Morley, F. H. W., Agricultural Gazette of New South Wales (Australia, Dominion of) 58: 660, 1947; 59: 263, 271, 1948.

2805. Shanes, A., The Journal of Pharmacology and Experimental Therapeutics 105: 216, 1952.

2806. Sharkey, T. P., and Simpson, W. M., The Journal of the American Medical Association 100: 97, 1933.

2807. Sharp, S. S., The Journal of Economic Entomology 39: 669, 1946.

2808. Shaw, F. R., The Journal of Economic Entomology 34: 16, 1941.

2809. Shaw, J. G., and Lopez, F., The Journal of Economic Entomology 47(5): 891, 1954.

2810. Shelanski, H. A., and Shelanski, M. V., Soap and Sanitary Chemicals 29(7): 129, 1953.

2811. Shelford, V. E., Bulletin No. 11 of the Illinois State Laboratory of Natural History, 1917.

2812. Shell Chemical Corporation, "Handbook of Aldrin, Dieldrin and Endrin Formulations", 1954.

2813. Shenefelt, R. D., The Journal of Economic Entomology 43: 684, 1950.

2814. Shepard, H. H., Nature (London) 134: 323, 1934.

2815. Shepard, H. H., "The Chemistry and Action of Insecticides", McGraw-Hill, New York, 1951.

2816. Shepard, H. H., et al., Minnesota Agricultural Experiment Station Technical Bulletin No. 120, 1937.

2817. Shepard, H. H., and Buzicky, A. W., The Journal of Economic Entomology 32(6): 854, 1939.

2818. Shepard, H. H., and Campbell, F. L., The Journal of Economic Entomology 25: 142, 1932.

2819. Shepard, H. H., and Carter, R. H., The Journal of Economic Entomology 26(4): 913, 1933.

2820. Shepherd, C. J., Nature (London) 170: 1073, 1952.

2821. Sherman, F., and King, H. L., The Journal of Economic Entomology 41: 807, 1948.

2822. Sherman, M., The Journal of Economic Entomology 41(4): 575, 1948.

2823. Sherman, M., and Norton, L. B., The Journal of Economic Entomology 41(2): 288, 1948.

2824. Sherman, M., and Rosenberg, M. M., The Journal of Economic Entomology 46(6): 1067, 1953.

2825. Ibid., 47(6): 1082, 1954.

2826. Sherrard, G. C., Public Health Reports (Washington, D.C.) 54: 2297, 1939.

2827. Shimkin, Proceedings of the Society for Experimental Biology and Medicine 34: 135, 1936.

2828. Shirley, D., U.S. Patent No. 2,472,269 (1949).

2829. Siakatos, N., The Journal of Economic Entomology 49(2): 212, 1956.

2830. Siegler, E. H., et al., The Journal of Economic Entomology 29: 532, 1936.

2831. Siegler, E. H., et al., U.S. Department of Agriculture Circular No. 523, 1939.

2832. Siegler, E. H., and Bowen, C., The Journal of Economic Entomology 39: 673, 1946.

2833. Siegler, E. H., and Gertler, S. I., The Journal of Economic Entomology 39: 662; 670, 1946.

2834. Silver, The Journal of Industrial Hygiene and Toxicology 30: 307, 1948.

2835. Silverman, M., and Abreu, B. E., University of California Publications in Pharmacology 1: 119, 1938.

2836. Simanton, W. A., quoted by Hansberry R., et al., in The Journal of Economic Entomology 33(3): 511, 1940.

2837. Simanton, W. A., and Miller, A., The Journal of Economic Entomology 30: 917, 1937.

2838. Simkover, H. G., and Shenefelt, R. D., The Journal of Economic Entomology 45(1): 11, 1952.

2839. Simmons, P., et al., U. S. Department of Agriculture Circular No. E-353, 1935.

2840. Simmons, P., and Ellington, G. W., Science 64: 326, 1926.

2841. Simms, B. T., Report of the Chief of the U.S. Bureau of Animal Industry for 1945 - 1946.

2942. Simonin, Comptes rendus des séances de la Société de biologie (Paris) 124: 133, 1937.

2843. Simpson, A. C., Nature (London) 155: 241, 1945.

2844. Skerrett, E., and Woodcock, D., Journal of the Chemical Society, 1950 p. 2718.

2845. Ibid., 1952, p. 3308.

2846. Skrjabina, E., Lenin All Union Academy of Agricultural Science (U.S.S.R.) Summary 1935/1936 p. 383.

2847. Skrjabina, E., Lenin All Union Academy of Agricultural Science (U.S.S.R.), Institute of Plant Protection, 1936.

2848. Slade, R. E., Chemistry and Industry, 1945 No. 40, p. 314.

2849. Slade, R. E., Endeavour (London) 4: 148, 1945.

2850. Slade, R. E., and Weed, A., Soap and Sanitary Chemicals 23: 115, 1947.

2851. Slagh, H., and Britton, E., Journal of the American Chemical Society 72: 2808, 1950.

2852. Slepyan, A. H., The Journal of the American Medical Association 124: 1127, 1944.

2853. Smallman, B. N., The Journal of Economic Entomology 42(4): 596, 1949.

2854. Smith, C., Journal of the American Chemical Society 53: 277, 1931.

2855. Ibid., 54: 397, 1932.

2856. Ibid., 57: 959, 1935.

2857. Smith, C., et al., The Journal of Economic Entomology 23: 863, 1930.

2858. Smith, C. F., The Journal of Economic Entomology 33: 724, 1940.

2859. Ibid., 41: 220, 1948.

2860. Smith, C. F., and Veerhoff, O., The Journal of Economic Entomology 40: 588, 1947.

2861. Smith, C. L., The Journal of Economic Entomology 41: 881, 1948.

2862. Smith, C. L., and Richards, R., The Journal of Economic Entomology 48(5): 566, 1955.

2863. Smith, C. N., and Gouck, H. K., The Journal of Economic Entomology 40: 790, 1947.

2864. Smith, E. H., et al., The Journal of Economic Entomology 49(1): 14, 1956.

2865. Smith, E. H., and Avens, A. W., The Journal of Economic Entomology 47(5): 912, 1954.

2866. Smith, E. H., and Wagenknecht, A. C., The Journal of Economic Entomology 49(6): 777, 1956.

2867. Smith, F. F., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D. C.

2868. Smith, F. F., Florists' Review 99: 31, 1947.

2869. Smith, F. F., The Journal of Economic Entomology 28(1): 91, 1935.

2870. Ibid., 41: 624, 1948.

2871. Ibid., 41: 955, 1948.

2872. Smith, F. F., et al., Agricultural Chemicals 2(12): 28, 1947.

2873. Ibid., 3(1): 37, 1948.

2874. Smith, F. F., et al., The Journal of Economic Entomology 38(2): 189, 1945.

2875. Ibid., 41: 624, 1948.

2876. Ibid., 43(5): 627, 1950.

2877. Ibid., 45: 703, 1952.

2878. Smith, F. F., and Brierly, P., Annual Review of Entomology 1: 299, 1956.

2879. Smith, F. F., and Goodhue, L. D., The Journal of Economic Entomology 38(2): 173, 1945.

2880. Smith, H. V., and Smith M. C., Arizona Agricultural Experiment Station Technical Bulletin No. 43, 1932.

2881. Smith, J., et al., Biochemical Journal (London) 54: 225, 1953.

2882. Smith, J. H., The Queensland Agricultural Journal (Australia, Dominion of) 61: 216, 1945.

2883. Smith, L. E., Industrial and Engineering Chemistry, Analytical Edition, 10: 60, 1938.

2884. Smith, L. E., Industrial and Engineering Chemistry 34(4): 499, 1942.
2885. Smith, L. E., The Journal of Economic Entomology 28: 727, 1935.
2886. Smith, L. E., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine No. E-399, 1937 (Mimeograph).
2887. Smith, L. E., and Melvin, R., The Journal of Economic Entomology 36(3): 475, 1943.
2888. Smith, M. C., and Leverton, R. M., Industrial and Engineering Chemistry 26: 791, 1934.
2889. Smith, M. I., et al., The Journal of Pharmacology and Experimental Therapeutics 60: 449, 1937.
2890. Ibid., 88: 359, 1946.
2891. Smith, M. I., et al., National Institutes of Health Bulletin (U.S.) No. 160, 1932.
2892. Smith, M. I., et al., Public Health Reports (Washington, D.C.) 45: 209, 1930.
2893. Ibid., 51: 1496, 1936.
2894. Smith, M. I., and Lillie, R. D., Archives of Neurology and Psychiatry (Chicago) 26: 976, 1931.
2895. Smith, M. I., and Stohlman, E. F., Public Health Reports (Washington, D.C.) 59: 984, 1944.
2896. Ibid., 60: 289, 1945.
2897. Smith, M. I., and Westfall, B. B., Public Health Reports 52: 1375, 1937.
2898. Smith, M. S., Annals of Applied Biology 35: 494, 1948.
2899. Smith, M. W., Transactions. The American Fisheries Society 69: 141, 1939.
2900. Smith, O. M., Water Works Engineering 97: 1293, 1944.
2901. Smith, R. F., et al., The Journal of Economic Entomology 41: 755, 1948.
2902. Smith, R. F., and Allen, W. W., The Journal of Economic Entomology 42: 487, 1949.
2903. Smith, R. H., The Journal of Economic Entomology 25(5): 988, 1932.
2904. Smith, R. H., et al., The Journal of Economic Entomology 27: 1192, 1934.
2905. Smith, W. A., The Queensland Agricultural Journal (Australia, Dominion of) 65: 315, 1947.
2906. Ibid., 66: 351, 1948.
2907. Smyth, Jr., H. F., Data on File; Chemical Hygiene Fellowship, Mellon Institute, Pittsburgh.
2908. Smyth, Jr., H. F., Archives of Industrial Hygiene and Occupational Medicine 4: 119, 1951.
2909. Smyth, H. F., et al., The Journal of Industrial Hygiene and Toxicology 18: 277, 1936.
2910. Smyth, H. F., and Carpenter, C. P., The Journal of Industrial Hygiene and Toxicology 30: 63, 1948.
2911. Smyth, H. F., and Smyth, Jr., Industrial and Engineering Chemistry 24: 229, 1932.
2912. Snapp, O. I., The Journal of Economic Entomology 32: 683, 1939.
2913. Ibid., 38: 417, 1945.
2914. Ibid., 40: 382, 1947.
2915. Ibid., 41: 7, 1949.
2916. Snapp, O. I., U.S. Department of Agriculture, Bureau of Entomology and Plant Quarantine Circular No. E-676, 1945.
2917. Snipes, B. T., Iowa State College Journal of Science 13: 93, 1938.
2918. Snipes, B. T., et al., The Journal of Economic Entomology 41: 635, 1948.
2919. Snyder, F. M., and Morton, F. A., The Journal of Economic Entomology 40: 586, 1947.
2920. Solaroli, V., and Bongiovanni G. C., L'Italia Agricola (Roma) 89: 479, 1952.
2921. Sollmann, T., "A Manual of Pharmacology", W. B. Saunders, Philadelphia 7th Edition, 1948.
2922. Sollmann, T., The Journal of Pharmacology and Experimental Therapeutics 14: 243, 1919.
2923. Soloway, S., and LaForge, F. B., Journal of the American Chemical Society 69: 979, 1947.
2924. Solvay and Company, British Patent No. 637,671 (1950).
2925. Soper, F. L., The American Journal of Tropical Medicine 6: 451, 1926.
2926. Soucek, B., et al., Archives of Industrial Hygiene and Occupational Medicine 6: 461, 1952 (Abstract).
2927. Southgate, B. A., Report; Department of Scientific and Industrial Research (Great Britain), Her Majesty's Stationery Office, London, 1948.
2928. Southgate, B. A., Report of the Water Pollution Research Board (Great Britain), 1950.
2929. Southgate, B. A., and Pentelow, F. T. K., Biochemical Journal (London) 26: 273, 1932.
2930. Späth, Berichte; Deutsche chemische Gesellschaft (Berlin) 70B: 70, 1937.
2931. Spealman, Industrial Medicine 14: 292, 1945.
2932. Spector, W. S., (Editor) Handbook of Toxicology, Volume I.
2933. Spencer, H. V., et al., Archives of Industrial Hygiene and Occupational Medicine 1: 341, 1950.
2934. Ibid., 4: 482, 1951.
2935. Spencer, H. V., et al., The Journal of Industrial Hygiene and Toxicology 30: 10, 1948.
2936. Speroni, G., Chimica e industria (Milano, Italia) 34: 391, 1952.
2937. Speroni, G., et al., Chimica e industria (Milano, Italia) 33: 209, 1951.
2938. Speyer, W., Zeitschrift für angewandte Entomologie (Berlin) 11: 395, 1925.
2939. Spicer, S. S., et al., Veterinary Medicine (Chicago) 42: 289, 1947.
2940. Spiegel, C. J., et al., Report MDDC - 1715, Atomic Energy Commission (U.S.), 1948.
2941. Spindler, M., Praxis (Bern) 38: 936, 1949.
2942. Spindler, M., Zeitschrift für Pflanzenkrankheiten (Pflanzenpathologie) und Pflanzenschutz (Stuttgart) 62: 97, 1955.
2943. Spolyar, L. W., Monthly Bulletin of the Indiana State Board of Health (Indianapolis) 52: 198, 1949.
2944. Srivastava, A. S., Indian Medical Record (Calcutta) 71: 43, 1951.
2945. Srivastava, A. S., Science 115: 403, 1952.
2946. Srivastava, A. S., and Wilson, H. F., The Journal of Economic Entomology 40(4): 569, 1947.
2947. Stafford, E. M., The Journal of Economic Entomology 42: 656, 1949.
2948. Stage, H. H., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
2949. Stark, F. L., Cornell University Agricultural Experiment Station Memoir No. 278, 1948.
2950. Starnes, F. B., and Granett, P., The Journal of Economic Entomology 46(3): 420, 1953.
2951. Starr, D., Soap and Sanitary Chemicals 26: 70, 1950.
2952. Starr, D., and Richardson, C. H., The Journal of Economic Entomology 29(1): 214, 1936.
2953. Stasney, J., and Higgins, G. M., Folia haematologica (Leipzig) 55: 93, 1936.

2954. State Water Pollution Control Board, "Water Quality Criteria", Publication No. 3, 1952 (Sacramento, California).

2955. Staudinger, H., and Ruzicka, L., Helvetica chimica acta (Basel) 7: 177, 1924.

2956. Ibid., 7: 212, 1924.

2957. Ibid., 7: 448, 1924.

2958. Stearns, Jr., C. R., et al., Citrus Magazine 13(13): 22, 1951.

2959. Stearns, L. A., et al., The Journal of Economic Entomology 40(1): 79, 1947.

2960. Ibid., 41: 264, 1948.

2961. Stedman, E., Biochemical Journal (London) 20: 719, 1926.

2962. Stedman, E., et al., Biochemical Journal (London) 26: 2056, 1932.

2963. Stegwee, D., Biochimica et biophysica acta (Amsterdam) 8: 187, 1952.

2964. Stehle, Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 104: 82, 1924.

2965. Steindorff, K., Archiv (Graefe's) für Opthalmologie (Berlin) 109: 252, 1922.

2966. Steiner, H. M., The Journal of Economic Entomology 28(2): 385, 1935.

2967. Steinweden, California State Department of Agriculture Bulletin 34(1): 5, 1945.

2968. Stellwag, F., and Staudenmayer, T., Anzeiger fur Schadlingskunde (Berlin) 16: 37, 1940.

2969. Stephens, R., Victoria, Australia (Dominion of) Department of Agriculture Journal 45: 468, 1947.

2970. Stephenson, O., and Waters, W., Journal of the Chemical Society, 1946, p. 339.

2971. Sternburg, J., et al., Journal of Agricultural and Food Chemistry 2(22): 1125, 1954.

2972. Sternburg, J., et al., The Journal of Economic Entomology 43: 214, 1950.

2973. Ibid., 46: 513, 1953.

2974. Sternburg, J., and Kearns, C. W., Annals of the Entomological Society of America 43: 444, 1950.

2975. Sternburg, J., and Kearns, C. W., The Journal of Economic Entomology 45(3): 497, 1952.

2976. Ibid., 45(3): 505, 1952.

2977. Ibid., 49(4): 548, 1956.

2978. Stevens, J., and Beutel, R., Journal of the American Chemical Society 63: 308, 1941.

2979. Stevenson, W. A., and Sheets, L. W., The Journal of Economic Entomology 39(1): 81, 1946.

2980. Steward, J. S., Nature (London) 158: 636, 1946.

2981. Stewart, J., and Smith, E. S., Soil Science, 14: 111, 1922.

2982. Steyn, D. G., Farming in South Africa 19(223): 649, 1944.

2983. St. John, J. L., et al., Journal of Agricultural Research 60: 317, 1940.

2984. Stoddard, E. M., Connecticut Agricultural Experiment Station Circular No. 160, 1944.

2985. Stohlman, E., Archives of Industrial Hygiene and Occupational Medicine 1: 13, 1950.

2986. Stohlman, E., Public Health Reports (Washington, D.C.) 66: 1303, 1951.

2987. Stohlman, E., and Smith, M. I., Advances in Chemistry Series 1: 228, 1950.

2988. Stoker, R. I., Annals of Applied Biology 35: 110, 1948.

2989. Stone, M. W., The Journal of Economic Entomology 35: 860, 1942.

2990. Ibid., 37(2): 297, 1944.

2991. Stone, M. W., U.S. Department of Agriculture Bulletin No. E-786, 1949.

2992. Stone, P. C., and Lahue, D. W., The Journal of Economic Entomology 39: 581, 1946.

2993. Stoner, R. D., and Hale, W. M., The Journal of Economic Entomology 46(4): 692, 1953.

2994. Stotz, E., et al., The Journal of Biological Chemistry (Baltimore) 124: 745, 1938.

2995. Strand, A. L., Industrial and Engineering Chemistry (Analytical Edition) 2: 4, 1930.

2996. Strand, A. L., Minnesota Agricultural Experiment Station Technical Bulletin No. 49, 1927.

2997. Straus, M., "Control of Weeds on Irrigation Systems", Bureau of Reclamation, U.S. Department of the Interior, Superintendent of Documents, 1949.

2998. Stringer, A., Annals of Applied Biology 36: 206, 1949.

2999. Ibid., 36: 213, 1949.

3000. Stubbings, W. A. K., Journal of the Entomological Society of Southern Africa (Pretoria, Union of South Africa) 8: 163, 1945.

3001. Sturge, and Whittaker, Biochemical Journal (London) 47: 518, 1950.

3002. Subba-Rao, N., and Pollard, A., Journal of the Science of Food and Agriculture 2: 462, 1951.

3003. Sullivan, W. N., et al., The Journal of Economic Entomology 34(1): 79, 1941.

3004. Ibid., 34: 650, 1941.

3005. Sullivan, W. N., et al., Soap and Sanitary Chemicals 14(9): 101, 1938.

3006. Ibid., 15(7): 107; 109; 111; 113, 1939.

3007. Sullivan, W. N., and Hornstein, I., The Journal of Economic Entomology 46(5): 898, 1953.

3008. Summerford, W. T., Journal of Agricultural and Food Chemistry 2(6): 310, 1954.

3009. Summerford, W. T., The Journal of the National Malaria Society (Tallahassee, Florida) 10: 345, 1951.

3010. Summerford, W. T., et al., Archives of Industrial Hygiene and Occupational Medicine 7: 383, 1953.

3011. Summerford, W. T., et al., Science 114: 6, 1951.

3012. Summers, F. M., The Journal of Economic Entomology 42(1): 22, 1949.

3013. Sun, Y. - P., Minnesota Agricultural Experiment Station Technical Bulletin No. 177, 1947.

3014. Sun, Y. - P., The Journal of Economic Entomology 43(1): 45, 1950.

3015. Sun, Y. - P., et al., The Journal of Economic Entomology 40: 366, 1948.

3016. Ibid., 41(1): 91, 1948.

3017. Ibid., 41(3): 366, 1948.

3018. Sundaram, S., Indian Coffee 16: 195, 1952.

3019. Surber, E. W., Journal of the American Water Works Association 42: 735, 1950.

3020. Surber, E. W., Progressive Fish- Culturist 10(3): 125, 1948.

3021. Surber, E. W., Water Pollution Abstracts No. 6, May 1933.

3022. Surber, E. W., and Friddle, D. D., Transactions. The American Fisheries Society 76: 315, 1946.

3023. Surber, E. W., and Hoffman, C. H., U.S. Department of the Interior, Fish and Wildlife Service Special Scientific Report No. 4, 1949.

3024. Svirbely, J. L., et al., The Journal of Industrial Hygiene and Toxicology 29: 382, 1947.

3025. Swaine, J. M., U.S. Department of Agriculture Bibliographic Bulletin No. 8, item 375, 1929.

3026. Sweetman, H. L., The Journal of Economic Entomology 40: 454, 1947.

3027. Sweetman, H. L., and Bourne, A. I., The Journal of Economic Entomology 37(2): 299, 1944.

3028. Sweetman, H. L., and Gyrisko, G. G., The Journal of Economic Entomology 37: 746, 1944.

3029. Sweetman, H. L., and Laudani, H., Soap and Sanitary Chemicals 18(4): 90, 1942.

3030. Swingle, D. B., and Morris, H. E., Photopathology 1: 79, 1911.

3031. Swingle, H. S., The Journal of Economic Entomology 31: 430, 1938.

3032. Swingle, M. C., et al., U.S. Department of Agriculture Bulletin Nos. E-548 and E-565, 1942.

3033. Ibid., Bulletin No. E-621, 1944.

3034. Ibid., Bulletin No. E-634, 1945.

3035. Swingle, M.C., and Cooper, J.F., The Journal of Economic Entomology 28: 220, 1935.

3036. Swiss, E. D., Proceedings of the Society of Experimental Biology and Medicine 76: 847, 1951.

3037. Symposium (Ist) on Chemical-Biological Coördination, National Research Council (U.S.) Publication No. 206, 1951.

3038. Synerholm, M. E., U.S. Patent No. 2,486,445 (1949).

3039. Synerholm, M. E., et al., Contributions from the Boyce Thompson Institute 13: 433, 1945.

3040. Ibid., 15: 35, 1947.

3041. Synerholm, M. E., and Hartzell, A., Contributions from the Boyce Thompson Institute 14(2): 79, 1945.

3042. Taggart, J. V., and Forster, R. P., The American Journal of Physiology 161: 167, 1950.

3043. Tahori, A. S., and Hoskins, W. M., The Journal of Economic Entomology 46: 302; 829, 1953.

3044. Taillade, M., Comptes rendus hebdomadaires des séances de l'Académie des sciences (Paris) 218: 836, 1944.

3045. Tainter, The Journal of Pharmacology and Experimental Therapeutics 53: 58, 1935.

3046. Takasaka, T., Zeitschrift für die gesamte gerichtliche Medizin 6: 488, 1926.

3047. Takei, S., and Miyajima, S., Oyo - Kontyu (Japan) 3: 59, 1941.

3048. Tamshiro, M., and Sherman, M., The Journal of Economic Entomology 48(1): 75, 1955.

3049. Tarasova, K., Izvestia Kurs Prikladnoi Zoologii 6: 15, 1936.

3050. Tarzwell, C. M., Public Health Reports (Washington, D.C.) 65(8): 231, 1950.

3051. Taschen, B., and Wirriger, W., Deutsche medizinische Wochenschrift (Leipzig) 75: 1478, 1950.

3052. Taschenberg, E. F., The Journal of Economic Entomology 43(1): 76, 1950.

3053. Tate, H. D., and Gates, R. A., The Journal of Economic Entomology 43(1): 152, 1950.

3054. Tattersfield, F., Annals of Applied Biology 17: 181, 1927.

3055. Tattersfield, F., et al., Annals of Applied Biology 12: 218, 1925.

3056. Ibid., 14: 217, 1927.

3057. Ibid., 43: 498, 1953.

3058. Tattersfield, F., et al., Journal of Agricultural Science 19: 266, 1929.

3059. Tattersfield, F., and Martin, J. T., Annals of Applied Biology 25: 411, 1938.

3060. Tattersfield, F., and Roberts, A. W. R., Annals of Applied Biology 10: 199, 1920.

3061. Tauber, E., Zentralblatt für die medizinischen Wissenschaften (Berlin) 18: 775, 1880.

3062. Taubmann, G., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 150: 257, 1930.

3063. Taylor, H., Chemical Industries 64: 314, 1945.

3064. Taylor, H., and Frodsham, J., Nature (London) 158: 558, 1946.

3065. Teichmann, W., and Heidsieck, B., Das Deutsche Gesundheitswesen (Berlin) 6: 1315, 1951.

3066. Telford, H. S., The Journal of Economic Entomology 40: 918, 1947.

3067. Telford, H. S., and Guthrie, J. E., The Journal of Economic Entomology 39(3): 413, 1946.

3068. Telford, H. S., and Guthrie, J. E., Science 102: 647, 1945.

3069. Telford, H. S., and Guthrie, J. E., Soap and Sanitary Chemicals 22: 124, 1946.

3070. Tenhet, J. E., The Journal of Economic Entomology 37(1): 147, 1944.

3071. Tennessee Department of Public Health and Industrial Hygiene, Tennessee Industrial Hygiene News 6: 1, 1949.

3072. Tew, R. P., and Kirby, A. H. M., Reports on the Progress of Applied Chemistry (The Society of Chemical Industry, London) XXXVIII 632, 1953.

3073. Therrien, A. A., et al., The Journal of Economic Entomology 47(1): 76, 1954.

3074. Thiemann, H. A., American Industrial Hygiene Association Quarterly 10: 10, 1949.

3075. Thiodet, J., et al., L'Algérie médicale (Algiers) 54: 95, 1950.

3076. Thiodet, J., et al., La Presse médicale (Paris) 58: 325, 1950.

3077. Thiodet, J., and Michaux, P., Archives des maladies professionelles; hygiène et toxicologie industrielles (Paris) 11: 594, 1950.

3078. Thomas, B. G. H., and Yant, W. P., Public Health Reports 42: 370, 1927.

3079. Thomas, E. F., Journal of Agricultural Research (Washington, D.C.) 45: 317, 1932.

3080. Thomas, E. F., and Shealy, A. L., Journal of Agricultural Research (Washington, D.C.) 45: 315, 1932.

3081. Thomas, W. D. E., and Bennett, S. H., Annals of Applied Biology 41: 501, 1954.

3082. Thome, H. J., Data on Methoxychlor contributed on behalf of the E. I. DuPont de Nemours Company, Grasselli Chemicals Department, 1956.

3083. Thompson, R. W., 76th Annual Report of the Entomological Society of Ontario (Canada, Dominion of), 1945.

3084. Thoms, H., and Thumen, S., Berichte; Deutsche chemische Gesellschaft 44: 3717, 1911.

3085. Thori, A. S., Chemical Abstracts 47: 813, 1953.

3086. Thornton, N. C., and Setterstrom, C., Contributions from the Boyce Thompson Institute 11: 343, 1940.

3087. Thorp, J., and de Meillon, B., Nature (London) 160: 264, 1947.

3088. Thoung, U. C., The Indian Medical Gazette (Calcutta) 81: 432, 1946.

3089. Thresh, J. C., and Beale, J. F., "The Examination of Waters and Water Supplies", Blakiston, 1925.

3090. Thurston, J., U.S. Department of Commerce, Field Information Agency Technical Final Report No. 949, 1946.

3091. Thurston, R., The Journal of Economic Entomology 46(4): 545, 1953.

3092. Tietz, H., Bayer Company Technical Bulletin, 1953.

3093. Tirelli, M., Tobacco (London) 56: 355, 1952.

3094. Tischler, N., The Journal of Economic Entomology 28: 215, 1935.
3095. Tobias, J. M., and Kollros, J. J., The Biological Bulletin 91: 247, 1946.
3096. Tobias, J. M., et al., The Journal of Cellular and Comparative Physiology 28: 159, 1946.
3097. Tobias, J. M., et al., The Journal of Pharmacology and Experimental Therapeutics 86: 287, 1946.
3098. Todd, F. E., et al., Agricultural Chemicals 4(8): 27, 1949.
3099. Todd, F. E., and McGregor, S. E., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.
3100. Tolkmith, H., Journal of the American Chemical Society 75: 5276, 1953.
3101. Topley, B., Chemistry and Industry, 1950, p. 859.
3102. Torda, C., and Wolff, H., The Journal of Pharmacology and Experimental Therapeutics 95: 444, 1949.
3103. Townson, W. K., The Veterinary Record (London) 50: 403, 1938.
3104. Toy, A. D. F., Journal of the American Chemical Society 70: 3882, 1948.
3105. Ibid., 72: 2065, 1950.
3106. Ibid., 73: 4670, 1951.
3107. Trappmann, W., Zeitschrift für Pflanzenkrankheiten (Pflanzenpathologie) und Pflanzenschutz 48: 514, 1938.
3108. Trappmann, W., and Nitsche, G., Mitteilungen aus der biologischen Reichsanstalt für Land- und Forst- wirtschaft No. 46, 1933-1935, p. 61.
3109. Trappmann, W., and Nitsche, G., Nachrichtenblatt für den deutschen Pflanzenschutzdienst 15: 6, 1935.
3110. Traub, R., et al., The Journal of Economic Entomology 47(3): 429, 1954.
3111. Travis, B. V., The Journal of Economic Entomology 31(6): 649, 1938.
3112. Ibid., 32(5): 706, 1939.
3113. Ibid., 36(1): 56, 1943.
3114. Ibid., 42(4): 451, 1949.
3115. Travis, B. V., and Bohart, R. M., The Journal of Economic Entomology 39(6): 740, 1946.
3116. Travis, B. V., and Smith, C. N., The Journal of Economic Entomology 44(3): 428, 1951.
3117. Travis, G. E., The Journal of Economic Entomology 36: 477, 1943.
3118. Trelease, S. F., and Trelease, H. M., American Journal of Botany 24: 448, 1937.
3119. Trelles, R. A., and Amato, F. D., Public Health Engineering Abstracts November/December 1950.
3120. Treon, J. F., et al., Journal of Agricultural and Food Chemistry 3(10): 842, 1955.
3121. Treon, J. F., et al., Report; Kettering Laboratory Department of Preventive Medicine and Industrial Health, University of Cincinnatti, College of Medicine, 1952.
3122. Ibid., Report of February 14, 1953.
3123. Ibid., Report of July 11, 1953.
3124. Ibid., Report of November 4, 1953.
3125. Ibid., Report of December 31, 1954.
3126. Ibid., Report of June 30, 1954.
3127. Ibid., Report of February 1, 1955.
3128. Treon, J. F., and Cleveland, F. P., Journal of Agricultural and Food Chemistry 3(5): 402, 1955.
3129. Tripod, J., Archives internationales de pharmacodynamie et de therapie (Paris) 74: 343, 1947.
3130. Tsao, C.-H., et al., The Journal of Economic Entomology 47(5): 796, 1954.
3131. Tsukamoto, M., and Ogaki, M., Botyu Kagaku (Kyoto) 18: 39, 1953.
3132. Tsuyuki, H., et al., Journal of Agricultural and Food Chemistry 3(11): 922, 1955.
3133. Tucker, R. P., Industrial and Engineering Chemistry 28: 458, 1936.
3134. Tunblad, B., Växtskyddsnotiser (Stockholm) 4: 49, 1952.
3135. Ibid., 5: 82, 1952.
3136. Turner, H. J., et al., Industrial and Engineering Chemistry 40: 450, 1948.
3137. Turner, N., Connecticut Agricultural Experiment Station Bulletin No. 576, 1953.
3138. Turner, N., The Journal of Economic Entomology 37(2): 242, 1944.
3139. Ibid., 44(1): 106, 1951.
3140. Turner, N., et al., Connecticut Agricultural Experiment Station Bulletin No. 521, 1948.
3141. Turner, N., and Bliss, C. I., Annals of Applied Biology 40: 79, 1953.
3142. Turner, N., and Woodruff, N., The Journal of Economic Entomology 41: 328, 1948.
3143. Ibid., 42: 470, 1949.
3144. Tusing, et. al., Journal of Agricultural and Food Chemistry 3(4): 312, 1955.
3145. Tutin, F., Annual Report of the University of Bristol (Great Britain) Agricultural and Horticultural Research Station at Long Ashton, 1927, p. 81.
3146. Tennessee Valley Authority, "Malaria Control on Impounded Water", U.S. Government Printing Office, 1947.
3147. Tzaturyan, G. B., Review of Applied Entomology (London) B36: 170, 1948.
3148. Uhry, P., and Marcel, G., Archives des maladies professionelles; hygiène et toxicologie industrielles (Paris) 11: 589, 1950.
3149. Unterstenhöfer, G., Hofchen-Briefe für Wissenschaft und Praxis (Bayer Pflanzenschutz Nachrichten) 6: 121, 1953.
3150. U.S. Department of Agriculture, Agricultural Research Service, Reprint from Federal Register of December 12, 1954, Plant Pest Control Branch-Pesticides Regulation Section.
3151. U.S. Department of Agriculture, Bulletin No. E-762, Review. Bureau of Entomology and Plant Quarantine, 1949.
3152. U.S. Department of Agriculture, Circular No. 380.
3153. U.S. Department of Agriculture, Farmers' Bulletin No. 1533.
3154. Ibid., No. 1880.
3155. U.S. Department of Agriculture, "Insects", The Yearbook of Agriculture 1952. U.S. Government Printing Office, Washington, D.C.
3156. U.S. Food and Drug Administration, Tolerance Hearings FDC-57 R. 7204-7205, 1950.
3157. United States Patent No. 1,893,081.
3158. Ibid., No. 2,070,603 (1937).
3159. Ibid., No. 2,400,295.
3160. Ibid., Nos. 2,418,458 and 2,418,459.
3161. Ibid., No. 2,420,928.
3162. Ibid., No. 2,464,600 (1949).
3163. Ibid., No. 2,482,063.
3164. Ibid., No. 2,505,699 (1950).
3165. Ibid., No. 2,550,737.
3166. U.S. Public Health Service Drinking Water Standards in Journal of the American Water Works Association 38: 361, 1946.
3167. Valade, P., Archives internationales de pharmacodynamie et de thérapie (Paris) 84: 360, 1950.

3168. Valade, P., and Salle, J., Bulletin de l'Académie vétérinaire de France (Paris) 23: 255, 1950.
3169. Van Asperen, K., and Oppenoorth, F. J., Nature (London) 173: 1000, 1954.
3170. Vandecayeye, S. C., et al., Soil Science 42: 203, 1936.
3171. Van den Bosch, R., et al., The Journal of Economic Entomology 49(3): 359, 1956.
3172. Van den Bruel, W. E., Parasitica 2: 129, 1946.
3173. Van der Laan, P. A., "Onderzoekingen over de Schuurvaat", Mededeeling. Deli Proef Station (Sumatra) No. 5, 1940.
3174. Van der Linden, L., Berichte; Deutsche chemische Gesellschaft 45: 231, 1912.
3175. Van Heusden, G. P. H., Water (The Netherlands) 32: 109, 1948.
3176. Van Horn, W. M., Paper Trade Journal 117(24): 33, 1943.
3177. Vaniev, A. D., Proceedings of the Lenin (All Union) Academy of Agricultural Science 16: 43, 1951.
3178. Van Leeuwen, E. R., U.S. Department of Agriculture Circular No. 227, 1932.
3179. Velbinger, H., Transactions of the VIIIth International Congress of Entomology 1948, p. 953.
3180. Verbeke, R., Archives internationales de pharmacodynamie et de thérapie 80: 19, 1949.
3181. Verma, J. S., The Journal of Economic Entomology 49(1): 58, 1956.
3182. Viado, G., Iowa State College Journal of Science 16: 146, 1941.
3183. Viel, G., Comptes rendus hebdomadaires des séances de l'Académie d'agriculture de France (Ministére d'Agriculture) 32: 804, 1946.
3184. Viel, G., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris 1952, p. 527.
3185. Viel, G., et al., Proceedings of the Second International Congress of Plant* Protection, London 1949, p. 487 (*also Crop).
3186. Viktorov, V. F., et al., Review of Applied Entomology (London) 1948, pp, 81; 130.
3187. Viles, F. J., The Journal of Industrial Hygiene and Toxicology 22: 188, 1940.
3188. Vincent, L. E., et al., The Journal of Economic Entomology 47: 943, 1954.
3189. Vinson, E. B., and Kearns, C. W., The Journal of Economic Entomology 45(3): 484, 1952.
3190. Vjshelesskaya (Vyshelesskaya), N. S., "Acid Sodium Arsenite as an Insecticide", Memoirs of the Poisonous Substances Research Laboratory, Part I, Leningrad 1927, edited by Zashchita Rasteniĭ ot Vreditelei (Bi͡ulleten Posto͡iannogo Bi͡uro Vserossiĭskikh Entomo-fitopatologicheskikh S″ezdov (Protection of Plants from Pests) in English at Library of Congress, Washington, D.C.
3191. Voegtlin, C., Physiological Review 5: 63, 1925.
3192. Voegtlin, C., et al., The Journal of Pharmacology and Experimental Therapeutics 25: 297, 1925.
3193. Voegtlin, C., et al., Public Health Reports (Washington, D.C.) 46: 339, 1931.
3194. Vogel, A., and Bloodgood, D. E., Proceedings of the Sixth Industrial Wastes Conference, 1951; (in The Purdue Engineering Bulletin).
3195. Vogelbach, C., Angewandte Chemie 63: 378, 1951.
3196. Voigt, Journal of the American Pharmaceutical Association 37: 122, 1948.
3197. Volck, W. H., California Agricultural Experiment Station Bulletin No. 153, 1903.
3198. Von Oettingen, W. F., Data in a personal communication to, from U.S. Food and Drug Administration.
3199. Von Oettingen, W. F., "The Halogenated Hydrocarbons, Toxicity and Potential Dangers", U.S. Department of Health, Education and Welfare, Public Health Service. U.S. Printing Office, Washington D.C., 1955.
3200. Von Oettingen, W. F., U.S. National Institutes of Health Bulletin No. 185, 1946.
3201. Von Oettingen, W. F., et al., The Journal of Industrial Hygiene and Toxicology 18: 310, 1936.
3202. Von Oettingen, W. F., et al., U.S. National Institutes of Health Bulletin No. 191, 1949.
3203. Von Oettingen, W. F., and Sharpless, N., The Journal of Pharmacology and Experimental Therapeutics 88: 400, 1946.
3204. Von Rümker, R., Data contributed on behalf of the Chemagro Corporation in January, 1956.
3205. Vorhaus, et al., Gastroenterology (Baltimore) 15: 304, 1950.
3206. Voskresenskaya, A. K., "On the Principles of the Resistance of Some Insects to Arsenic Insecticides" (Summary in English, text in Russian). Leningrad Institut. Zashchita rasteniĭ No. 19 pp. 132-144, 1939. (Library of Congress).
3207. Voskresenskaya, A. K., Review of Applied Entomology (London) A27: 310, 1939.
3208. Voskresenskaya, A. K., "The Penetration of Poisons through the Intestinal Wall of Insects" (in Russian). Leningrad Institut Zashchity Rasteniĭ. Trudy po zashchite rasteniĭ Series III No. 7 pp. 25-37, 1936. (Library of Congress).
3209. Wachs, H., Science 105 : 530, 1947.
3210. Wachs, H., et al., Advances in Chemistry Series 1: 43, 1950.
3211. Wachtel, C., "Chemical Warfare", Chemical Publishing Company, Brooklyn, New York 1941.
3212. Wagner-Jauregg, T., et al., Journal of the American Chemical Society 73: 5202, 1951.
3213. Waite, Public Health Reports (Washington, D.C.) 45: 1832, 1930.
3214. Wakeland, C., and Parker, J. R., in "Insects". The Yearbook of Agriculture 1952, U.S. Department of Agriculture, Washington, D.C.
3215. Waldman, R. K., et al., Archives of Industrial Hygiene and Occupational Medicine 9: 37, 1954.
3216. Walker, H. W., and Miller, J. E., Industrial and Engineering Chemistry 19: 703, 1927.
3217. Walker, K. C., et al., Journal of Agricultural and Food Chemistry 2(20): 1034, 1954.
3218. Wallace, C. R., Agricultural Gazette of New South Wales (Australia, Dominion of) 59: 435, 1948.
3219. Wallace, C. R., Journal of the Australian Institute of Agricultural Science 13: 132, 1948.
3220. Wallace, P. P., The Journal of Economic Entomology 44(2): 224, 1951.
3221. Walton, R. R., The Journal of Economic Entomology 39(2): 273, 1946.
3222. Ibid., 40: 389, 1947.
3223. Wandell, W. N., Illinois Custom Spray Operator's School Outline (Urbana, Illinois) 1949.
3224. Warburg, O., Zeitschrift für physiologische Chemie (Hoppe-Seylers) (Leipzig) 70: 413, 1911.
3225. Warburg, O., Science 123: 309, 1956.
3226. Ward, A. A., and Wheatley, M. D., Journal of Neuropathology and Experimental Neurology (Baltimore) 6: 292, 1947.
3227. Ward, J. C., Chemistry and Industry 1953, p. 586.
3228. Ward, J. C., Agricultural Chemicals 1(8): 24, 1946.

3229. Ward, J. C., The Journal of the American Medical Association 158: 1364, 1955.

3230. Ward, J. C., and DeWitt, J. B., Pests 16(3): 34, 1948.

3231. Warrick, L. F., Engineering News-Record 124: 34, 1940.

3232. Warrick, L. F., Proceedings of the Sixth Industrial Waste Conference, 1951, p. 455. (Conference dates: February 21 - 23).

3233. Warrick, L. F., Waterworks and Sewerage 90: 269, 1943.

3234. Wason, E. J., Agricultural Gazette of New South Wales (Australia, Dominion of) 56: 498, 1945.

3235. Wason, E. J., and Lloyd, N. C., Agricultural Gazette of New South Wales (Australia, Dominion of) 59: 538, 1948.

3236. Waterhouse, D., Australia (Dominion of), Council of Scientific and Industrial Research Bulletin No. 218, 1947, p. 7.

3237. Water Pollution Research Board (Great Britain), Report, 1947 (in Sewage Works Journal 21: 755, 1949).

3238. Waters, H. A., et al., The Journal of Economic Entomology 32(1): 144, 1939.

3239. Watkins, T. C., The Journal of Economic Entomology 35(2): 234, 1942.

3240. Watrous, R. M., The Journal of Industrial Hygiene and Toxicology 25: 35, 1943.

3241. Watson, E. B., and Thompson, R. W., Department of Agriculture, Canada (Dominion of) Division of Entomology, Publication No. 36, 1948.

3242. Watts, C. N., and Berlin, F. D., The Journal of Economic Entomology 43(3): 371, 1950.

3243. Waugh, G. D., et al., Annals of Applied Biology 39: 407, 1952.

3244. Way, M. J., Annals of Applied Biology 36: 86, 1949.

3245. Ibid., 41: 77, 1954.

3246. Way, M. J., Bulletin of Entomological Research (London) 40: 279, 1949.

3247. Way, M. J., and Synge, A. D., Annals of Applied Biology 35(1): 94, 1948.

3248. Weaver, N., The Journal of Economic Entomology 42(6): 973, 1949.

3249. Ibid., 43(2): 353, 1950.

3250. Webb, E., Biochemical Journal (London) 42: 96, 1948.

3251. Webb, J., Bulletin of Entomological Research (London) 36: 15, 1945.

3252. Webb, J., and Green, R., The Journal of Experimental Biology (London) 22: 9, 1945.

3253. Weber, E., Zeitschrift (Fresenius') für analytische Chemie (Wiesbaden, München) 132: 26, 1951.

3254. Webster, R. L., The Journal of Economic Entomology 26: 1016, 1933.

3255. Webster, R. L., Washington (State of) Agricultural Experiment Station Circular No. 64, 1948.

3256. Wedding, R. T., and Metcalf, R. L., California Citrograph 38: 138, 1953.

3257. Wedding, R. T., Journal of Agricultural and Food Chemistry 1(13): 832, 1953.

3258. Weed, A., Soap and Sanitary Chemicals 14(6): 133, 1938.

3259. Weedon, F. R., et al., Contributions from the Boyce Thompson Institute 10: 281, 1939.

3260. Weigel, C. A., U.S. Department of Agriculture Circular No. 380, 1926.

3261. Weigel, C. A., and St. George, R. A., in "Insects". The Yearbook of Agriculture 1952. U.S. Department of Agriculture, Washington, D.C.

3262. Wieland, Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 97: 489, 1923.

3263. Weinman, C. J., The Journal of Economic Entomology 40: 567, 1947.

3264. Weinman, C. J., et al., The Journal of Economic Entomology 40; 91, 1947.

3265. Weinman, C. J., and Decker, G. C., The Journal of Economic Entomology 40(1): 74, 1947.

3266. Ibid., 40(1): 84, 1947.

3267. Ibid., 42(1); 135, 1949.

3268. Ibid., 44(4): 547, 1951.

3269. Weismann, R., Mitteilungen aus der biologischen Bundesanstalt für Land-und Forstwirtschaft (Braunschweig) No. 83, p. 17, 1954.

3270. Weismann, R., Verhandlungen. Schweizerische naturforschende gesellschaft (Société helvetique des sciences naturelles, Genéve) 126: 166, 1946.

3271. Weismann, R., et al., Experientia 7: 117, 1951.

3272. Weismann, R., et al., Proceedings of the XIIth International Congress of Pure and Applied Chemistry.

3273. Weismann, R., and Kocher, C., Zeitschrift für angewandte Entomologie (Berlin) 33: 297, 1951.

3274. Weiss, J. M., and Downs, C. R., Industrial and Engineering Chemistry 15: 1022, 1923.

3275. Wells, R. W., and Barrett, W. L., The Journal of Economic Entomology 39: 816, 1946.

3276. Welsh, Archives internationales de pharmacodynamie et de thérapie (Paris) 14: 211, 1905.

3277. Welsh, H., The Journal of Economic Entomology 41(1): 36, 1948.

3278. Welsh, J., and Gordon, H. T., The Journal of Cellular and Comparative Physiology 30: 147, 1947.

3279. Wene, G. P., The Journal of Economic Entomology 40: 675, 1947.

3280. Ibid., 41: 514, 1948.

3281. Ibid., 42: 73, 1949.

3282. Wene, G. P., and White, A. N., The Journal of Economic Entomology 45(1): 118, 1952.

3283. Werle, E., et al., Biochemische Zeitschrift (Berlin) 320: 189, 1950.

3284. Werle, E., and Koebke, K., Justus Liebig's Annalen der Chemie (Leipzig) 562: 60, 1949.

3285. Werle, E., and Meyer, A., Biochemische Zeitschrift (Berlin 321: 221, 1950.

3286. West, T., Pyrethrum Post 2(2): 16, 1951.

3287. West, T. F., and Campbell, G. A., "DDT, the Synthetic Insecticide", Chapman and Hall, London 1946.

3288. West, T. F., Verhandelingen; Eerste International Congres voor Phytopharmacie, Heverlee (Nederlands) 1946, p. 193.

3289. Westgate, R. A., and Raynor, R. N., California Agricultural Experiment Station Bulletin No. 634, 1940.

3290. Whitaker, Physiological Review 31: 312, 1951.

3291. Whitcomb, W. D., Massachusetts Agricultural Experiment Station Bulletin No. 326, 1935.

3292. White, W. C., and Sweeney, T. R., Public Health Reports (Washington, D.C.) 60: 66, 1945.

3293. Whitehead, F. E., The Journal of Economic Entomology 47(4): 676, 1954.

3294. Whitnall, A. B. M., Bulletin of Entomological Research (London) 38: 353, 1949; 40: 207, 1951.

3295. Wiersma, C. A., and Schallek, W., Science 106: 241, 1947.

3296. Wigglesworth, V. B., The British Medical Journal 1: 517, 1945.

3297. Wigglesworth, V. B., Bulletin of Entomological Research (London) 33: 205, 1942.
3298. Wigglesworth, V. B., The Journal of Experimental Biology (London) 21: 97, 1945.
3299. Wigglesworth, V. B., Nature (London) 147: 116, 1941.
3300. Ibid., 153: 493, 1945.
3301. Wigglesworth, V. B., Proceedings of the Cambridge Philosophical Society 6: 181, 1931.
3302. Wilbur, D. A., The Journal of Economic Entomology 45(6): 913, 1952.
3303. Wilcox, J., and Howland, A. F., The Journal of Economic Entomology 41: 694, 1948.
3304. Ibid., 49(2): 242, 1956.
3305. Wilcox, W., The British Medical Journal 1: 105, 1945.
3306. Wilhelm, G., and Domenjoz, R., Archives internationales de pharmacodynamie et de thérapie (Paris) 86: 321, 1951.
3307. Wilks, L. P., Data (without bibliography) contributed in October, 1955.
3308. Williams, C. L., Public Health Reports (Washington, D.C.) 49: 192, 1934.
3309. Williams, E., Industrial and Engineering Chemistry 43: 950, 1951.
3310. Williams, J. R., Annual Report; Department of Agriculture, Mauritius (Island of) 1952, p. 59.
3311. Williams, J. W., The Journal of the Florida Medical Association (Jacksonville) 37: 293, 1950.
3312. Williams, J. W., and Griffith, J. T., The Journal of the Florida Medical Association (Jacksonville) 37: 707, 1951.
3313. Willis, J. A., The Biological Bulletin 48: 209, 1925.
3314. Wills, J. H., et al., Federation Proceedings 9: 136, 1950.
3315. Wilson, The Journal of the American Medical Association 139(14): 906, 1949.
3316. Wilson, et al., The Journal of Clinical Investigation 31: 815, 1952.
3317. Wilson, C. A., Thesis; University of California, 1936.
3318. Wilson, C. S., The Journal of Economic Entomology 42: 423, 1949.
3319. Wilson, H., and Barker, J., 126th Meeting of the American Chemical Society; Abstracts No. 74, p. 29A, 1954.
3320. Wilson, H. G., et al., The Journal of Economic Entomology 46(4): 699, 1953.
3321. Wilson, H. G., and Gahan, J. B., Science 107: 276, 1948.
3322. Wilson, I., and Cohen, M., Biochimica et biophysica acta (Amsterdam) 11: 147, 1953.
3323. Wilson, I., and Meislich, E., Journal of the American Chemical Society 75: 4628, 1953.
3324. Wilson, J. D., and Sleesman, J. P., Ohio Agricultural Experiment Station Bimonthly Bulletin No. 32, 1947 p. 58.
3325. Wilson, J. K., Journal of Agricultural Research (Washington, D.C.) 77: 25, 1948.
3326. Wilson, J. W., Proceedings of the Florida Horticultural Society, 1951, p. 117.
3327. Wilson, M. C., The Journal of Economic Entomology 42: 496, 1949.
3328. Wilson, R. E., and De Eds, F., The Journal of Industrial Hygiene and Toxicology 18: 553, 1936.
3329. Wilson, R. W., and Brumley, D. R., Industrial Medicine 13: 233, 1944.
3330. Wilson, S. G., Bulletin of Entomological Research (London) 39: 428, 1948.
3331. Wingo, C., The Journal of Economic Entomology 47(4): 632, 1954.
3332. Winteringham, F. P. W., Bulletin; National Research Council (U.S.) Publication No. 219, 1952, p. 61.
3333. Winteringham, F. P. W., Compte Rendu; III^{me} Congrès international de phytopharmacie, Paris, 1952.
3334. Winteringham, F. P. W., Nature (London) 166: 999, 1950.
3335. Winteringham, F. P. W., Science 116: 452, 1952.
3336. Ibid., 116: 482, 1952.
3337. Winteringham, F. P. W., Department of Scientific and Industrial Research, Pest Infestation Research p. 36, 1952.
3338. Winteringham, F. P. W., Journal of the Science of Food and Agriculture 7: 214, 1950.
3339. Winteringham, F. P. W., and Harrison, A., Journal of the Society of Chemical Industry (London) 65(5): 140, 1946.
3340. Wirtschafter, Z. T., and Schwartz, E. D., The Journal of Industrial Hygiene and Toxicology 21: 126, 1939.
3341. Wisecup, C. B., et al., The Journal of Economic Entomology 39(1): 52, 1946.
3342. Wisecup, C. B., and Deonier, C. C., The Journal of Economic Entomology 38(2): 250, 1945.
3343. Witherspoon, M. G., and Garber, C. Z., U.S. Chemical Warfare Service D3, Report E.A.M.R., 1922.
3344. Witman, E. D., et al., The Journal of Economic Entomology 32(1): 142, 1939.
3345. Witt, P., Zeitschrift für Naturforschung (Wiesbaden) 2b: 361, 1947.
3346. Woglum, R. S., et al., The Journal of Economic Entomology 40: 818, 1947.
3347. Woke, P. A., Journal of Agricultural Research (Washington, D.C.) 57: 707, 1938.
3348. Ibid., 58: 289, 1939.
3349. Ibid., 61: 321, 1940.
3350. Wolcott, G. N., The Journal of Economic Entomology 40(1): 24, 1947.
3351. Ibid., 40(1): 27, 1947.
3352. Ibid., 42(2): 273, 1949.
3353. Ibid., 44(2): 263, 1951.
3354. Wolcott, G. N., Review of Applied Entomology A36: 169, 1948.
3355. Wolfenbarger, P. O., The Journal of Economic Entomology 41: 818, 1948.
3356. Wolfenbarger, P. O., Proceedings of the Florida Horticultural Society, 1952, p. 197.
3357. Wolfsie, J. H., and Winter, G. D., Archives of Industrial Hygiene and Occupational Medicine 6: 43, 1952.
3358. Woodard, G., et al., Federation Proceedings 7: 266, 1948.
3359. Woodard, G., et al., Industrial and Engineering Chemistry 40: 711, 1948.
3360. Woodard, G., et al., The Journal of Pharmacology and Experimental Therapeutics 82: 152, 1944.
3361. Woodard, G., et al., Science 102 : 177, 1945.
3362. Woodard, G., and Hagan, E. C., Federation Proceedings 6: 386, 1947.
3363. Woodard, G., and Ofner, R. R., Federation Proceedings 5: 215, 1946.
3364. Woodburg, E. N., Agricultural Chemicals 4(3): 31, 1949.

3365. Woodcock, D., and Stringer A., Annals of Applied Biology 38: 111, 1951.

3366. Woodside, A. M., The Journal of Economic Entomology 41: 722, 1948.

3367. Ibid., 42: 63, 1949.

3368. Ibid., 42: 335, 1949.

3369. Woodstock, W., U.S. Patent No. 2,402,703 (1946).

3370. Woodworth, Journal of Agricultural Research (Washington, D.C.) 57: 229, 1938.

3371. Wooldridge, W. E., Journal of Investigative Dermatology (Baltimore) 10: 363, 1948.

3372. Worthington, A. D., and Decker, G. C., The Journal of Economic Entomology 29: 760, 1936.

3373. Worthley, H. N., and Steiner, H. M., The Journal of Economic Entomology 32: 278, 1939.

3374. Ibid., 35(1): 102, 1942.

3375. Wright, D. W., and Geering, Q. A., Bulletin of Entomological Research (London) 39: 57, 1948.

3376. Wright, J. M., and Decker, G. C., The Journal of Economic Entomology 48(3): 250, 1955.

3377. Wright, W. H., et al., The Journal of the American Medical Association 109: 570, 1937.

3378. Wright, W. H., and Schaffer, J. M., The American Journal of Hygiene 16: 325, 1932.

3379. Wyllie, J., Canadian Public Health Journal (Toronto) 28: 128, 1937.

3380. Yates, W., and Lindquist, A. W., The Journal of Economic Entomology 43: 653, 1950.

3381. Yeager, J. F., Journal of Agricultural Research (Washington, D.C.) 56: 267, 1938.

3382. Yeager, J. F., et al., Annals of the Entomological Society of America 28: 256, 1935.

3383. Ibid., 35: 23, 1942.

3384. Yeager, J. F., and Gahan, J., Journal of Agricultural Research 55: 1, 1937.

3385. Yeager, J. F., and Munson, S. C., Annals of the Entomological Society of America 38: 559, 1945.

3386. Yeager, J. F., and Munson, S. C., Science 102: 305, 1945.

3387. Young, H. B., and Busbey, R. L., U.S. Department of Agriculture 1935.

3388. Young, H. C., The Journal of Economic Entomology 37(1): 145, 1944.

3389. Young, H. D., et al., The Journal of Economic Entomology 28: 1049, 1935.

3390. Young, H. D., and Cotton, R. T., The Journal of Economic Entomology 36(5): 796, 1943.

3391. Young, L. A., and Nicholson, H. P., Progressive Fish-Culturist 13(4): 193, 1951.

3392. Young, P. A., Journal of Agricultural Research (Washington, D.C.) 49: 559, 1934.

3393. Young, P. A., and Morris, H. E., Journal of Agricultural Research (Washington, D.C.) 47: 505, 1933.

3394. Yust, H. R., et al., The Journal of Economic Entomology 35(3): 339, 1942.

3395. Yust, H. R., and Busbey, R. L., The Journal of Economic Entomology 35(3): 343, 1942.

3396. Zangger, H., Sammlung von Vergiftungsfällen (Fühner - Wielands) unter Mitwirkung der Deutschen pharmakologischen Gesellschaft 5: A195, 1934.

3397. Zeid, M., et al., The Journal of Economic Entomology 46: 324, 1953.

3398. Zimmerman, P. W., and Crocker, W., Contributions from the Boyce Thompson Institute 6: 455, 1935.

3399. Zimmerman, P. W., and Hartzell, A., Contributions from the Boyce Thompson Institute 15: 11, 1947.

3400. Zobrist, L., Verhandelingen; Eerste Internationaal Congrés voor Phytopharmacie, Heverlee (Nederlands) 1946.

3401. Zoepffel, R., Archiv für experimentelle Pathologie und Pharmakologie (Leipzig) 49: 89, 1903.

3402. Zollinger, F., Archiv für Gewerbepathologie und Gewerbehygiene (Berlin) 2: 298, 1931.

3403. Zukel, J., The Journal of Economic Entomology 37: 796, 1944.

3404. Zupko, A. G., and Edwards, L. D., Journal of the American Pharmaceutical Association 38: 124, 1949.

INDEX OF SCIENTIFIC AND COMMON NAMES

Note: The numbers following the entries indicate the Section in which the entry occurs.

A

Acanthopsyche junodi (wattle bagworm), 42
Acanthoscelides (=*Bruchus*) *obtectus* (bean weevil), 1; 28; 37; 861; 87; 88; 89; 101; 104; 114; 121; 122
Acarina, 15; 30; 77; 110; 175
Acariscus mansoni (=*Eutrombicula alfreddugesi*) (Chiggers, jiggers, red bug), 14; 30; 102; 110; 140
Acellus aquaticus (Crustacea), 154
Aceratogallia sanguinolenta (clover leafhopper), 154; 157
Acer saccharum (plant), 117; 145; 183
Aceria paradianthi, 178
Aceria sheldoni (citrus bud mite), 15; 24; 35; 36; 53; 55; 75; 85; 126
Acomatocarus australiensis, 114
Acyrthosiphum pisi, 134; 179
Adalia bipunctata (two-spotted lady beetle), 17
Adelges, 157
Adelphocoris rapidus (rapid plant bug), 159
Aëdes, 17; 73; 81; 91; 95; 96; 108; 114; 120; 138; 156; 171
Aëdes aegypti (yellow fever mosquito), 2; 3; 10; 13; 16; 17; 30; 41; 48; 73; 91; 95; 103; 106; 107; 114; 120; 132; 134; 135; 137; 138; 140; 154; 155; 158; 159; 171
Aëdes (Alaskan sp.), 155
Aëdes dorsalis, 2; 17; 56; 81; 108; 183
Aëdes nigromaculis, 17; 69; 93; 134; 180
Aëdes nigromaculis, DDT-R biotype, 93; 117; 180
Aëdes sollicitans (salt marsh mosquito), 17; 48; 73; 91; 103; 156
Aëdes taeniorhynchus, 13; 17; 48; 56; 73; 91; 103; 114; 138; 155; 156
Aëdes taeniorhynchus, DDT-R biotype, 138; 156
Aëdes vexans (swamp mosquito), 2; 17; 56; 81; 183
Aegeria (=*Sanninoidea; Canopia*) *exitiosa* (peach tree borer), 49; 88; 138; 150
Aesclepias syriaca (plant), 130
Aesculaceae (plant family), 149
Aesculus californica (plant), 149
Aesculus parviflora (plant), 117; 145
African mosquito. see Anopheles gambiae
Agelastica alni 154; 157
Agriotes (genus of beetles), 23; 49; 104
Agriotes mancus (wheat wireworm), 13
Agromyza phaseoli (French bean fly), 130
Agropyron repens (plant), 170
Agrotis, 154; 157
Agrotis orthogonia (pale western cutworm), 17; 30; 76; 114; 130; 154; 183
Agrotis segetum, 154
Ahasverus, 173
Ailanthus (plant genus), 149
Alabama argillacea (cotton leafworm), 7; 13; 25; 30; 60; 65; 66; 67; 112; 134; 139; 183
Aleurocanthus woglumi (Citrus blackfly), 138
Alfalfa,
  caterpillar. see *Colias* (=*Eurymus*) *eurytheme*
  weevil. see *Hypera postica*
Allium cepa (plant), 114; 170
Allograpta obliqua, 59
Allotropa, 17
Almond moth. see *Ephestia cautella*
Alnus glutinosa (plant), 145
Alsophila pometaria (Fall cankerworm), 50; 112
Altica ambiens, 134
Altica bimarginata, 13
Amaranthus retroflexus (plant), 170
Ambylomma americanum (lone star tick), 13; 47; 48; 56; 73; 91; 96; 103; 138; 183
Amblyomma maculatum (Gulf Coast tick), 48
Ambrosia artemisiifolia (plant), 170
American,
  cockroach. see *Periplaneta americana*
  dog tick. see *Dermacentor variabilis*
Amianthium muscaetoxicum (plant), 149
Amphorophora rubi, 18; 132; 172
Anabasis aphylla (plant), 149
Anabrus simplex (Mormon cricket), 162
Anagasta kühniella, 170
Anarsia lineatella (peach twig borer), 112
Anasa, 134
Anasa tristis (squash bug), 2; 7; 13; 17; 30; 56; 81; 93; 108; 114; 130; 132; 134; 138; 149; 154; 157; 158; 159; 161; 183
Anastrepha ludens (mexican fruit fly), 13; 30; 87
Anastrepha mombinpraeoptans (mango fly), 87
Ancylis comptana (strawberry leaf roller), 11
Ancylostoma duodenale (Nematohelminthes), 177
Andrena (a genus of wild bees), 13; 17
Angoumois grain moth. see *Sitotraga cerealella*
Annonaceae (plant family), 149
Annona reticulata (plant), 149
Annona squamosa (plant), 149
Anomala, 2
Anomala orientalis (oriental beetle), 13; 45; 114
Anopheles, 17; 19; 120; 142; 156
Anopheles albimanus, 17
Anopheles crucians, 17; 61; 69; 93; 134; 180
Anopheles gambiae (African mosquito), 13
Anopheles maculipennis, 13
Anopheles quadrimaculatus (common malaria mosquito), 2; 3; 13; 16; 17; 19; 30; 48; 56; 61; 69; 73; 91; 93; 96; 103; 108; 114; 117; 120; 125; 128; 134; 137; 138; 140; 142; 147; 154; 157; 178; 179; 180; 183
Ant,
  Argentine. see *Iridomyrmex humilis*
  black carpenter. see *Camponotus pennsylvanicus*
  fire. see *Solenopsis geminata*
  imported fire. see *Solenopsis saevissima*
  pharaoh. see *Monomorium pharaonis*
  red harvester. see *Pogonomyrmex barbatus*
Anthocoris musculus, 17
Anthocoris nemorum, 17
Anthomyids, 118
Anthonomus eugenii (pepper weevil), 188
Anthonomus grandis (boll weevil), 2; 13; 17; 25; 30; 56; 60; 65; 66; 67; 69; 70; 114; 130; 134; 173; 183
Anthonomus pomorum, 13; 23; 77
Anthonomus pyri, 13; 77
Anthonomus signatus (strawberry weevil), 13; 30; 42; 112; 168; 183
Anthrenoceros australasiae, 184
Anthrenus, 114
Anthrenus scrophulariae (common carpet beetle), 129
Anthrenus vorax (furniture carpet beetle), 29; 88; 89; 104; 127
Anticarsia, 173
Anticarsia gemmatilis (velvetbean caterpillar), 7; 13; 25; 30; 40; 42; 120; 138; 157; 158; 173; 183
Antirrhinum (plant genus), 166; 179
Anuraphis, 75
Anuraphis crataegi, 132
Anuraphis helichrysi, 132
Anuraphis padi, 18
Anuraphis rosae, 59; 77; 157
Anuraphis tulipae, 59; 132
Anystis agilis, 17
Aonidiella, 23; 124
Aonidiella aurantii (California red scale), 17; 28; 37; 87; 89; 94; 96; 101; 104; 117; 122; 124; 156; 178; 184
Aonidiella aurantii, HCN-nonR and HCN-R biotypes (strains), 101; 122; 156; 184
Aonidiella aurantii, Methyl bromide - R strain, 122
Aonidiella citrina (yellow scale), 17; 113
Apantesis phyllira, 157
Apantesis proxima, 17; 96
Aphaenogaster, 112
Aphelinus mali, 17; 141
Aphid,
  apple. see *Aphis pomi*
  apple-grain. see *Rhopalosiphum prunifoliae*
  bean. see *Aphis fabae*
  black citrus. see *Toxoptera aurantii*
  buckthorn. see *Aphis abbreviata*
  cabbage. see *Brevicoryne brassicae*
  cane. see *Aphis sacchari*
  chrysanthemum. see *Macrosiphoniella sanborni*
  corn leaf. see *Aphis maidis*
  cotton. see *Aphis gossypii*
  cowpea. see *Aphis medicaginis*
  crescent-marked lily. see *Myzus circumflexus*
  green citrus. see *Aphis spiraecola*
  green peach. see *Myzus persicae*
  hop (hopvine). see *Phorodon humuli*
  mealy plum. see *Hyalopterus arundinis*
  melon. see *Aphis gossypii*
  pea. see *Macrosiphum pisi*
  potato. see *Macrosiphum solanifolii*
  primrose. see *Pemphigus auriculae*
  rose. see *Macrosiphun rosae*
  strawberry. see *Capitophorus fragaefolii*
  strawberry root. see *Aphis forbesi*
  sugarbeet root. see *Pemphigus betae*
  turnip. see *Rhopalosiphum pseudobrassicae*
  walnut. see *Chromaphis juglandicola*
  woolly apple. see *Eriosoma lanigerum*
Aphids. see *Amphorophora, Anuraphis, Aphis, Brevicoryne, Capitophorus, Chaitophorus, Chromaphis, Drepanosiphum, Eriosoma, Hyalopterus, Illinoia, Macrosiphoniella, Macrosiphum, Masonaphis, Myzus, Myzodes, Neomyzaphis, Pemphigus, Phorodon, Phylloxera, Rhopalosiphoninum, Rhopalosiphum, Sapphaphis, Toxoptera*
Aphidius brassicae, 18; 20; 132
Aphidius phorodontis, 130
Aphis, 30; 59; 70; 77; 111; 113; 130; 172
Aphis abbreviata, (buckthorn aphid), 76
Aphis, cane. see *Aphis sacchari*
Aphis forbesi, (strawberry root aphid), 59; 130
Aphis gossypiella, 59
Aphis gossypii (melon aphid; cotton aphid), 17; 59; 60; 65; 66; 130; 132; 134; 138; 157; 168; 183
Aphis ideae, 132
Aphis maidis (corn leaf aphid), 17; 166
Aphis medicaginis (cowpea aphid), 132
Aphis persicae-niger, 30; 157
Aphis pomi (apple aphid), 5; 20; 59; 61; 63; 76; 100; 109; 132; 134; 137; 138; 141; 143; 157; 158
Aphis rumicis, 5; 26; 72; 76; 78; 109; 117; 130; 131; 134; 135; 138; 141; 143; 154; 157; 159

Aphis sacchari (cane aphis), 132
Aphis sambuci, 109
Aphis sorbi, 157
Aphis spiraecola (green citrus aphid), 17; 23; 76
Aphrophora (spittlebugs), 30; 138
Aphthona virescens, 13
Aphytis mytilaspidis, 17
Apion, 13
Apis, 106; 134; 137; 149; 163; 180
Apis indica, 13; 17
Apis mellifera (honeybee), 2; 7; 8; 12; 13; 16; 17; 18; 25; 30; 42; 46; 55; 56; 59; 72; 76; 77; 78; 85; 88; 93; 94; 96; 100; 112; 114; 117; 120; 125; 130; 132; 134; 137; 138; 142; 143; 149; 154; 157; 158; 159; 161; 163; 165; 168; 173; 178; 179; 180; 183
Apis mellifica. see *Apis mellifera*
Apocynaceae (plant family), 149
Apple,
  aphid. see *Aphis pomi*
  curculio. see *Tachypterellus quadrigibbus*
  grain aphid. see *Rhopalosiphum prunifoliae*
  leafhopper. see *Typhlociba comes*
  maggot. see *Rhagoletis pomonella*
  oyster-shell scale. see *Lepidosaphes ulmi*
  redbug. see *Lygidea mendax*
Appleworm. see *Carpocapsa pomonella*
Archips (=*Cacoecia*) *argyrospila* (fruit tree leaf roller), 96
Arctia caja, 143
Areca (plant), 122
Argasidae (argasid ticks; family of arthropods), 154
Argas persicus (fowl tick), 117
Argentine ant. see *Iridomyrmex humilis*
Argyrotaenia, 16
Argyrotaenia citrana (orange tortrix), 16; 42; 138
Argyrotaenia velutinana (red-banded leaf roller), 16; 30; 112; 120; 138; 179; 183
Arizona brown stink bug. see *Euschistus impictiventris*
Armadillidium nosatum (pill bug; sowbug), 17
Armyworms. see *Cirphis unipuncta, Prodenia eridania*
Artemia salina (brine shrimp; Crustacea), 30; 114; 120; 183
Asagraea officinalis (plant). see *Schoenocaulon officinale*
Ascaris (Nematohelminthes), 177
Ascia (=*Pieris*) *rapae* (imported cabbageworm), 7; 11; 25; 42; 50; 77; 78; 139; 142
Asclepias syriacus (plant), 170
Ascogaster, 112
Ash tree borer. see *Podesesia syringae fraxini*
Asparagus sprengeri plumosa (plant), 179
Aspidiotus, 113
Aspidiotus camelliae (greedy scale), 122
Aspidiotus cyanophylli (cyanophyllum scale), 122
Aspidiotus lataniae (Latania scale), 122
Aspidiotus perniciosus, lime-sulfur tolerant biotype, 156
Aspidiotus perniciosus (San José scale), 20; 75; 77; 89; 101; 104; 113; 122; 132
Assassin bug. see *Rhodnius prolixus*
Aster leafminer. see Liriomyza flaveola
Astragulus (plant genus), 166
Athalia spinarum, 154; 157
Attagenus, 114
Attagenus piceus (black carpet beetle), 9; 28; 29; 30; 37; 50; 88; 89; 96; 104; 122; 127; 129; 169; 170
Aulocorthum circumflexum, 18
Aulocorthum solani, 18
Australian,
  banana thrip. see *Scirtothrips signipennis*
  lady beetle. see *Rodolia cardinalis, Cryptolaemus montrouzieri*
  beet webworm. see *Hymenia recurvalis*
Australorbis glabratus (mollusc; snail), 140
Autographa brassicae, 25; 42; 50; 157
Autographa ♂♂, 188
Avena sativa (plant), 170

B

Baccha clavata, 59
Bagworm. see *Thyridopteryx ephemeraeformis*
Banana thrips (Australian). see *Scirtothrips signipennis*
Banded greenhouse thrips. see *Hercinothrips femoralis*
Bdellonyssus sylviarum (northern fowl mite), 117
Bean,
  aphid. see *Aphis fabae*
  leaf beetle. see *Cerotoma trifurcata*
  thrips. see *Hercothrips fumipennis*
  weevil (common). see *Acanthoscelides obtectus, Bruchus obtectus*
Bed bugs. see *Cimex* spp.
Bees, carpenter. see *Xylocopa violacea*
Bees. see *Andrena, Bombus agrorum, B. pratorum, B. terrestris, Apis mellifera, A. indica, Xylocopa violacea*
Beet,
  leafhopper. see *Circulifer* (=*Eutettix*)
  webworm. see *Loxostege sticticalis*
Beetle(s),
  bean leaf. see *Cerotoma trifurcata*
  black blister. see *Epicauta pennsylvanica*
  black carpet. see *Attagenus piceus*
  blister. see Blister beetles
  cadelle. see *Tenebrioides mauritanicus*
  Cantharis. see *Cantharis consors*
  carpet. see *Anthrenus scrophulariae, Anthrenus vorax, Attagenus piceus*
  cerambycid. see *Cerambycid beetles*
  cigarette. see *Lasioderma serricorne*
  Colorado potato. see *Leptinotarsa decemlineata*
  confused flour. see *Tribolium confusum*
  cucumber (spotted). see *Diabrotica undecimpunctata*
  dried fruit. see *Carpophilus hemipterus*
  drug store. see *Stegobium paniceum*
  elm leaf. see *Galerucella xanthomelaena*
  flea. see Flea beetles
  grain. see Grain beetles
  green June. see *Cotinis nitida*
  Japanese. see *Popillia japonica*
  lady. see Lady beetles
  larder. see *Dermestes lardarius*
  May beetle. see Melolontha vulgaris
  Mexican bean. see *Epilachna varivestis*
  mountain pine. see *Dendroctonus monticolae*
  oriental. see *Anomala orientalis*
  powder post. see *Lyctus* (genus), *Ptinus* (genus)
  red flour. see *Tribolium castaneum*
  red-legged ham. see *Necrobia rufipes*
  spotted cucumber. see *Diabrotica undecimpunctata*
  white-fringed. see *Pantomorus* (=*Graphognathus*) *leucoloma*
Begonia (plant genus), 141
Begonia incarnata (plant), 122
Begonia rex (plant), 122
Beta vulgaris (plant), 170
Birch leaf-miner. see *Fenusa pusilla*
Biscirus australicus, 17
Blabera fusca, 2; 30; 56; 81; 96; 108
Blaberus cranifer, 158
Black,
  beetle of New South Wales. see *Heteronychus sanctaehelenae*
  blister beetle. see *Epicauta pennsylvanica*
  blow fly. see *Phormia regina*
  carpenter ant. see *Camponotus pennsylvanicus*
  citrus aphid. see *Toxoptera aurantii*
  cricket (common). see *Gryllus assimilis*
  flies. see *Simulium* genus and spp. thereof
  scale. see *Saissetia oleaë*
  widow spider. see *Latrodectus mactans*
Blackfly, citrus. see *Aleurocanthus woglumi*
Blatta, 8; 17; 21; 23; 37; 69
Blatta germanica, 173
Blatta orientalis (Oriental cockroach), 3; 7; 13; 30; 50; 135; 154; 163; 167
Blattella, 1; 21; 23; 69; 132; 134; 138; 147; 156; 163; 173
Blattella germanica (German cockroach), 2; 3; 6; 9; 13; 17; 19; 30; 50; 56; 61; 76; 77; 94; 103; 106; 114; 117; 130; 142; 144; 146; 154; 156; 158; 163; 167; 170; 173; 179; 182; 183
Blattella germanica, Chlordane non-R strain, 114; 156; 179
Blattella germanica, chlordane-R strain, 2; 3; 17; 56; 61; 92; 114; 156; 179
Blattella germanica, Chlordane-S strain, 2; 56; 96; 114; 156; 179
Blattella germanica, Corpus Christi biotype (Chlordane-R), 30; 56; 96; 114; 156
Blattella germanica, DDT-R, 17; 56; 61; 156
Blattella germanica, non-R, 17; 61; 156
Blepharidopterus angulatus, 31
Blissus, 30; 159
Blissus hirtus (hairy chinch bug), 2
Blissus leucopterus (chinch bug), 26; 76; 77; 96; 141; 158
Blister beetles. see *Cantharis consors, Epicauta pennsylvanica*
Blowfly, black. see *Phormia regina*
Bluebottle flies. see *Calliphora erythrocephala, C. vomitoria*
Bluebug. see *Argas persicus*
Blue fever tick. see Boōphilus decoloratus
Blunt-nosed cranberry leafhopper. see *Scleroracus vaccinii*
Body lice, 128
Body louse, human. see *Pediculus humanus corporis*
Boisduval's scale. see *Diaspis boisduvalii*
Bollweevil. see *Anthonomus grandis*
Bollworm, 13. see also *Heliothis armigera*
Bollworm, pink. see *Pectinophora gossypiella*
Bomb fly. see *Hypoderma bovis*
Bombus agrorum (a bumblebee), 13; 17
Bombus pratorum (a bumblebee), 13; 17
Bombus terrestris (a bumblebee), 13; 17
Bombyx mori (silkworm, domesticated), 7; 8; 11; 25; 39; 41; 42; 75; 76; 77; 78; 94; 112; 130; 142; 154; 157; 158; 162; 163; 165
Boōphilus, 13; 17
Boōphilus decoloratus (fever tick), 13; 130; 162
Boōphilus (=*Margaropus*) *annulatus* (fever tick), 13
Boōphilus microplus (fever tick), 114
Boraginaceae (plant family), 149
Borer,
  ash tree. see *Podosesia syringae fraxini*
  clover root. see *Hylastinus obscurus*
  flatheaded apple tree. see *Chrysobothris femorata*
  lesser grain. see *Rhizopertha (=Rhyzopertha) dominica*
  lilac. see *Podosesia syringae syringae*
  peach tree. see *Sanninoidea (=Aegeria) exitiosa;* also see *Aegeria exitiosa*
  peach twig. see *Anarsia lineatella*
  roundheaded apple tree. see *Saperda candida*
  sugarcane moth. see *Diatraea saccharalis*
Bot flies. see *Gasterophilus*
Bot fly, human. see *Dermatobia hominis*
Bougainvillea (plant genus), 170
Bovicola bovis (=Trichodectes scalaris), 30
Bovicola caprae (goat louse), 17; 61; 69; 74; 93; 117; 134; 167
Bovicola limbatus, 17; 61; 69; 74; 93; 117; 134; 167
Boxwood leaf miner. see *Monararthropalpus buxi*
Brachycaudis helichrysi, 100; 109; 138
Brachyrhinus, 165
Brachyrhinus ligustici, 30; 122; 138; 183
Brassica rapa (plant), 170
Bregmatothrips iridis (Iris thrips), 130
Bremisia tabaci, 17
Brevia brassicae, 157
Brevicoryne brassicae (cabbage aphid), 17; 18; 20; 59; 100; 109; 130; 132; 138; 157; 179
Brevipalpus, 10; 138
Brevipalpus lewisi, 85
Brine shrimp. see *Artemia salina*
Broad mite. see *Hemitarsonemus latus*
Bromus inermis (plant), 170
Brown scale. see *Eulecanium corni*
Bruchus (=Acanthoscelides) obtectus (bean weevil), 28; 37; 88; 104; 129
Bruchus (=Mylabris) pisorum (pea weevil), 188
Bruchus sinensis, 37
Bryobia, 72
Bryobia praetiosa (clover mite), 15; 17; 24; 35; 36; 53; 54; 55; 59; 93; 126; 138
Bryobia pratensis, 130
Bucculatrix thurberiella, 60; 65; 66
Buckthorn aphid. see *Aphis abbreviata*
Bud moth, eye spotted. see *Spilonota ocellana*
Budworm,
  spruce. see *Choristoneura fumiferana*
  tobacco. see *Heliothis virescens*
Bug(s),
  apple red. see *Lygidea mendax*
  assassin. see *Rhodnius prolixus*
  bed. see *Cimex* spp.
  chinch. see *Blissus leucopterus*
  damsel. see *Nabis, Nabis ferus*
  hairy chinch. see *Blissus hirtus*
  harlequin. see *Murgantia histrionica*
  kissing. see *Triatoma*
  lace. see *Corythuca*
  lygus. see *Lygus* spp.

Note: The numbers following the entries indicate the Section in which the entry occurs.

Bug(s), *(Continued)*
  milkweed. see *Oncopeltus fasciatus*
  rapid plant. see *Adelphocoris rapidus*
  squash. see *Anasa tristis*
  stink. see *Euschistus impictiventris, Chlorochroa sayi, Nezara viridula*
  tarnished plant. see *Lygus oblineatus*
Bulb mite. see *Rhyzoglyphus echinopus*
Bumblebees. see *Bombus* spp.
Buxus (plant genus), 166

C

Cabbage,
  aphid. see *Brevicoryne brassicae*
  leafhopper. see *Trichoplusia ni*
  maggot. see *Hylemya brassicae*
Cabbage worm, imported. see *Pieris (=Ascia) rapae; Ascia rapae*
Cabbageworms. see *Ascia rapae, Diataraxia oleracea, Evergestis rimosalis, Mamestra picta, Pieris rapae*
Cacoecia cerasivorana, 130
Cadelle (cadelle beetle). see *Tenebrioides mauritanicus*
Calandra granaria (=Sitophilus granarius, q.v.*)*, (granary weevil), 13; 17; 104
Calanthes (plant genus), 169
Calathus, 112
Calceolaria (plant genus), 141
Calendula (plant genus), 141
Calico black. see *Murgantia histrionica*
California red scale. see *Aonidiella aurantii*
Calliphora, 13; 114
Calliphora erythrocephala (blue bottle fly), 13; 17; 30; 130; 134; 154; 183
Calliphora vomitoria (blue bottle fly), 17; 154
Calliptamus, 7; 94; 163
Callitroga hominivorax (screwworm), 61; 188. also see *Cochliomyia (=Callitroga) americana*
Callosobruchus maculatus (cowpea weevil), 52
Camellia (plant), 122
Camellia scale. see *Lepidosaphes camelliae*
Camnula pellucida (clear-winged grasshopper), 2; 56; 162
Camponotus pennsylvanicus (=C. herculaneus pennsylvanicus) (black carpenter ant), 30
Campylomma verbasci, 17
Cane aphis. see *Aphis sacchari*
Cankerworm,
  Fall. see *Alsophila pometaria*
  Spring. see *Paleacrita vernata*
Cannaceae (plant family), 149
Cantharis beetle. see *Cantharis consors*
Cantharis consors (Cantharis beetle, blister beetle); 17
Capitophorus braggii, 76
Capitophorus fragaefolii,(strawberry aphid), 17; 18
Carassius auratus (goldfish), 168
Carassius morosus (fish), 17
Carpenter bee. see *Xylocopa violacea*
Carpenterworm(s). see *Prionoxystus robiniae, P. macmurtrei*
Carpet beetle(s). see *Anthrenus scrophulariae, Anthrenus vorax, Attagenus piceus*
Carpocapsa, 17; 94; 142; 149
Carpocapsa pomonella (codling moth, appleworm), 5; 11; 13; 16; 25; 30; 34; 42; 50; 82; 96; 103; 112; 120; 122; 125; 130; 138; 141; 142; 156; 157; 158; 162; 163; 183; 188
Carpophilus, 114
Carpophilus hemipterus (dried fruit beetle), 94
Carrot rust fly. see *Psila rosae*
Carum carvi (plant), 149
Carya ovata (plant), 117; 145
Case bearer insects. see *Coleophora* spp.
Casebearer, larch. see *Coleophora laricella*
Case-making clothes moth. see *Tinea pellionella*
Castanea dentata (plant), 149
Castor bean tick. see *Ixodes ricinus*
Catalpa sphinx. see *Ceratomia catalpae*
Caterpillar,
  alfalfa. see *Colias philodice eurytheme*
  eastern tent. see *Malacosoma americanum*
  salt-marsh. see *Estigmene acraea*
  velvetbean. see *Anticarsia gemmatalis*
  walnut. see *Datana integrrima*
  yellow-necked. see *Datana ministra*
Cat flea. see *Ctenocephalides felis*
Cattle,
  follicle mite. see *Demodex bovis*
  louse (biting or little red). see *Bovicola bovis*
  mange mite. see *Psoroptes bovis*
  tick. see *Boöphilus annulatus*
Cattleya (plant genus), 178
Celastraceae (plant family), 149
Celery leaf tier. see *Phlyctaenia rubigalis*
Cephus cinctus (wheat stem sawfly), 23; 30; 114
Cerambycid beetles, 140
Ceratitis capitata (Mediterranean fruitfly), 27; 72; 109; 137; 143
Ceratomia, 112
Ceratomia catalpae (catalpa sphinx), 7; 40; 41; 112; 130; 154; 157; 161
Cercis canadensis (plant), 145
Cercopidae (insect family), 50
Cerotoma trifurcata (bean leaf beetle), 120
Chafer, rose. see *Macrodactylus subspinosus*
Chaitophorus populi, 117; 134; 138
Chalcodermus aeneus (cowpea curculio), 30; 42; 183
Chamaecyparis obtusa (plant), 160
Chaoborus, 142
Chaoborus astictopus (Clear Lake gnat), 16; 46; 77; 142; 154; 157
Chaoborus punctipennis, 17
Cheimatobia brumata, 13
Chenopodiaceae (plant family), 149
Cherry fruit fly (flies). see *Rhagoletis cingulata, Rhagoletis fausta*
Cherry leafminer. see *Profensuia canadensis*
Chicken,
  louse (body). see *Eomenacanthus stramineus*
  mite. see *Dermanyssus gallinae*
Chiggers. see *Acariscus mansoni, Eutrombicula alfreddugesi, Trombicula irritans*
Chinch bug(s). see *Blissus leucopterus, Blissus hirtus*
Chionaspis, 75
Chionaspis furfura (scurfy scale), 77
Chironomus, 5; 8; 37; 49; 141; 154; 157
Chlorochroa sayi (Say stink bug), 13; 76; 77; 100
Chlorochroa uhleri, 30; 76; 114
Chorioptes bovis, 13; 114
Choristoneura (=Archips, Cacoecia) fumiferana (spruce budworm), 17; 25; 30; 76; 112; 114; 130; 154
Chortoicetes, 30
Chorythuca arcuata, 114
Chromaphis juglandicola (walnut aphid), 17; 59; 138; 156; 179
Chrysanthemum (plant genus), 179; 184
Chrysanthemum aphid. see *Macrosiphoniella sanborni*
Chrysanthemum cinerariaefolium (plant), 149; 154
Chrysanthemum coccineum (plant), 154
Chrysobothris femorata (flatheaded apple tree borer), 49; 129
Chrysocus auritus, 157
Chrysomelidae (insect family), 50
Chrysomphalus, 138
Chrysomphalus aonidum (Florida red scale), 23; 122
Chrysomphalus (=Aonidiella) aurantii (California red scale), 89. also see *Aonidiella aurantii*
Chrysomphalus dictyospermi (palm or dictyospermum scale), 141
Chrysomphalus ficus, 17
Chrysopa, 12; 17; 183
Chrysopa oculata (golden-eye lace wing, aphid lion), 59
Chrysopa rufilabris (lace-winged fly; aphid lion), 59
Chrysopa vulgaris (lace-winged fly; aphid lion), 59
Chrysops discalis (horse flies), 2; 17; 30; 50; 56; 61; 69; 81; 93; 96; 108; 114; 117; 120; 134; 183
Cicada (=Magicicada), 179
Cicada (=Magicicada) septendecim (seventeen year locust), 100; 138; 179
Cicadellid leafhoppers, 77
Cigarette beetle. see *Lasioderma serricorne*
Cimex, 23; 69; 104; 154; 171
Cimex lectularius (bed bug), 1; 13; 14; 16; 17; 19; 23; 29; 33; 37; 51; 52; 88; 89; 90; 101; 104; 106; 111; 114; 120; 121; 122; 135; 146; 154; 169; 171; 176; 182; 183; 184; 186
Cimex rotundatus (bed bug), 89
Cineraria (plant genus), 184
Circulifer (=Eutettix) tenellus (beet leafhopper), 154
Cirphis, 16; 30; 165
Cirphis unipuncta (armyworm), 2; 7; 13; 17; 25; 30; 56; 67; 77; 78; 112; 114; 120; 134; 138; 139; 162; 165; 183
Citricola scale. see *Coccus pseudo-magnoliarum*
Citrophilus mealy bug. see *Pseudococcus gahani*
Citrus (plant genus), 172
Citrus,
  blackfly. see *Aleurocanthus woglumi*
  bud mite. see *Aceria sheldoni*
  mealybug. see *Pseudococcus citri*
  red mite. see *Paratetranychus citri*
  rust mite. see *Phyllocoptruta oleivora*
  white fly. see *Dialeurodes citri*
Cladastris lutea (plant), 117; 145
Clausenia purpurea, 17
Clear Lake gnat. see *Chaoborus astictopus*
Clear winged grasshopper. see *Camnula pellucida*
Clothes moth,
  case making. see *Tinea pellionella*
  webbing. see *Tineola bisselliella*
Clothes moth. see *Tinea pellionella, Tineola bisselliella, Trichophaga tapetzella*
Clover,
  leafhopper. see *Aceratogallia sanguinolenta*
  mite. see *Bryobia practiosa*
  root borer. see *Hylastinus obscurus*
  root curculio. see *Sitona hispidula*
  weevil (red). see *Tychius griseus*
Clusiaceae (plant family), 149
Clysia ambiguella (European vine moth), 13; 25; 112
Coccinella septempunctata (a lady beetle), 17; 18; 20; 132
Coccinella undecempunctata (a lady beetle), 59
Coccus hesperidum (soft scale; tortoise scale), 17; 138; 178
Coccus pseudo-magnoliarum (citricola scale), 87; 89; 101
Coccus pseudo-magnoliarum, Methyl bromide-R strain, 122
Cochliomyia, 142
Cochliomyia americana, phenothiazine resistant biotype, 142; 156
Cochliomyia (=Callitroga) americana=Callitroga hominivorax, q.v. (screw-worm), 10; 79; 142
Cochliomyia (=Callitroga) macellaria) secondary screw-worm, 106; 142
Cochlospermaceae (plant family), 149
Cochlospermum gossypium (plant), 149
Cockroach,
  American. see *Periplaneta americana*
  German. see *Blattella germanica*
  Oriental. see *Blatta orientalis*
Cockroaches. see *Blabera, Blaberus, Blatta, Blattella, Periplaneta, Leucophaea*
Codling moth. see *Carpocapsa pomonella*
Coleomegilla maculata (a lady beetle), 12; 17; 50; 56; 59; 61; 69; 81; 93; 96; 117; 138; 167; 183
Coleophora laricella (larch casebearer), 113
Coleus sp. (plant), 122
Colias (=Eurymus) eurytheme=Colias philodice eurytheme (alfalfa caterpillar), 179
Collops vittatus, 12; 17; 50; 61; 69; 81; 96; 117; 138; 167; 183
Colorado potato beetle. see *Leptinotarsa decemlineata*
Common,
  black cricket. see *Gryllus assimilis*
  body louse (of poultry). see *Menopon gallinae*
  carpet beetle. see *Anthrenus scrophulariae*
  cattle grub. see *Hypoderma lineatum*
  dry-wood termite. see *Kalotermes minor*
  malaria mosquito. see *Anopheles quadrimaculatus*
Compositae (plant family), 149
Comstock mealy bug. see *Pseudococcus comstocki*
Confused flour beetle. see *Tribolium confusum*
Conium maculatum (plant), 149
Conodermus, 30; 114
Conopia extiosa. see *Aegeria exitiosa, Sanninoidea exitiosa*
Conotrachelus nenuphar (plum curculio), 13; 30; 50; 51; 56; 93; 96; 114; 117; 120; 134; 138; 183
Convergent lady beetle. see *Hippodamia convergens*
Convolvulus (plant genus), 176
Conwentzia, 17
Coriandrum sativum (plant), 149
Corethra, 154
Corn,
  borer, European. see *Pyrausta nubilalis*
  earworm. see *Heliothis armigera*
  field ant. see *Lasius americanus*
  leaf aphid. see *Aphis maidis*
  rootworm. see *Diabrotica longicornis*
Cornus amomum (plant), 117; 145

Note: The numbers following the entries indicate the Section in which the entry occurs.

Corynetes, 114
Corythuca ulmi (a lace bug), 130
Cosmos (plant genus), 135
Cotinis nitida (green June beetle), 51; 96; 138; 183
Cotinus coggygria (plant), 117; 145
Cotton fleahopper. see *Psallus seriatus*
Cotton leafworm, 13. also see *Alabama argillacea*
Cottony cushion scale. see *Icerya purchasi*
Cowpea,
  aphid. see *Aphis medicaginis*
  curculio. see *Chalcodermus aeneus*
  weevil. see *Callosobruchus maculatus*
Crab louse. see *Phthirus pubis*
Cracca (=Tephrosia, q.v.) (plant genus), 149
Cranberry,
  leafhopper, blunt-nosed. see *Scleroracus vaccinii*
  fruitworm. see *Mineola vaccinii*
Crassula (plant genus), 117
Crataegus cordata (plant), 117
Crataegus phaenopyrum (plant), 145
Crematogaster, 18
Creontiades femoralis, 13
Crescent-marked lily aphid. see *Myzus circumflexus*
Cricket,
  common black. see *Gryllus assimilis*
  Mormon. see *Anabrus simplex*
Criocoris, 112
Criocoris saliens, 17
Cross-stripped cabbageworm. see *Evergestis rimosalis*
Croton tiglium (plant), 149
Cryptolaemus montrouzieri (Australian lady beetle), 101
Cryptotermes brevis, 174
Ctenicera aereipennis destructor, 14; 114
Ctenocephalides, 13
Ctenocephalides felis (cat flea), 2; 73; 91; 96
Cucumber beetle, spotted. see *Diabrotica undecimpunctata*
Cucurbitaceae (plant family), 149
Cucurbita moschata (plant), 183
Cucurbita pepo (plant), 149; 183
Cucurbita sativus (plant), 170
Culex, 17; 141; 142; 156; 157
Culex molestus, 13
Culex pipiens (northern house mosquito), 5; 17; 106; 130; 135; 157
Culex pyrenaicus, 17
Culex quinquefasciatus (southern house mosquito), 2; 17; 69; 132; 157
Culex tarsalis, 17; 93; 117; 134
Culex tarsalis, DDT-R strains, 69; 93; 180
Culex territans, 157
Curculio,
  apple. see *Tachypterellus quadrigibbus*
  clover root. see *Sitona hispidula*
  cowpea. see *Chalcodermus aeneus*
  plum. see *Conotrachelus nenuphar*
Curculio caryae, 112
Currant sawfly. see *Pteronus ribesii*
Currantworm, imported. see *Nematus ribesii*
Cutworms. see *Agrotis, Feltia, Lycophotia, Peridroma*
Cyanophyllum scale. see *Aspidiotus cyanophylli*
Cyclamen (plant genus), 122
Cyclamen mite. see *Tarsonemus pallidus*
Cyclocephala, 96
Cyclocephala borealis, 96
Cycloneda sanguinea (a lady beetle), 59
Cylas, 13
Cylas formicarius (=Cylas formicarius elegantulus) (sweet potato weevil), 25; 30; 42; 139
Cyllene robiniae, 49
Cynaeus angustus, 170
Cynthia (=Vanessa, q.v.*) cardui* (painted lady), 77; 78; 157
Cyrtorhinus mundulus, 17; 59; 132; 134

D

Dacus, 87
Dacus cucurbitae (melon fly), 109; 130; 137; 143
Dacus dorsalis (Oriental fruit fly), 2; 17; 28; 29; 30; 32; 52; 82; 86; 87; 88; 89; 90; 96; 101; 104; 109; 120; 122; 124; 134; 137; 143; 151; 185
Dacus orientalis, 104
Damalinia, 163
Damalinia bovis, 13; 114
Damalinia canis, 13; 114
Damsel bugs. see *Nabis, Nabis ferus*
Daphnia magna (Crustacea), 21; 140; 161; 163
Dark mealworm. see *Tenebrio obscurus*
Dasyneura tetensis, 132
Datana integerrima (walnut caterpillar), 112; 130
Datana ministra (yellow-necked caterpillar), 7; 112; 157
Datana perspicua, 79; 112
Delphinium consolida (plant), 149
Deltocephalus (=Dacus) cucurbitae, 27; 72
Deltocephalus (=Dacus) dorsalis, 27; 72
Demodex bovis (Cattle follicle mite), 13
Dendroctonus monticolae (mountain pine beetle), 120; 183
Dendrolimus pini, 154; 157
Deraeocoris fasciolus, 17
Dermacentor andersoni (Rocky Mountain wood tick), 13
Dermacentor variabilis (American dog tick or wood tick), 47
Dermanyssus gallinae (chicken mite or poultry mite), 13; 117; 138
Dermatobia hominus (human bot fly), 13
Dermestes, 114
Dermestes lardarius (larder beetle), 13
Dermestes vulpinus, 13
Derris (plant genus), 157
Derris elliptica (plant), 149; 157
Derris malaccensis (plant), 149; 157
Desert mite. see *Septanychus desertorum*
Deutzia scabra (plant), 117; 145
Diabrotica, 130
Diabrotica duodecimpunctata (=Diabrotica undecimpunctata, q.v.*)* (spotted cucumber beetle), 7; 11; 13; 25; 30; 114; 120; 138; 157; 183
Diabrotica longicornis (corn rootworm), 2; 114
Diabrotica melanocephala, 11; 13
Diabrotica undecimpunctata (=Diabrotica duodecimpuntata, q.v.) (spotted cucumber beetle), 59
Diabrotica virgifera (Western corn rootworm), 114
Diabrotica vittata, 130
Diaeretus rapae, 17
Dialeurodes citri (citrus white fly), 23
Diamond-back moth. see *Plutella maculipennis*
Diaphania hyalinata (melonworm), 13; 112; 188
Diaphania nitidalis (pickleworm), 16; 114
Diaphnidia pellucida, 17
Diaspis, 138
Diaspis boisduvalii (Boisduval's scale), 26; 122
Diataraxia oleracea, 17; 76; 112; 114; 134; 138; 154; 157; 179
Diatraea saccharalis (sugarcane moth borer), 13; 30; 42; 158
Dichapetalum cymosum (Giftblaar plant), 164
Differential grasshopper. see *Melanoplus differentialis*
Digitaria sanguinalis (plant), 170
Diorymerellus, 122
Diparopis watersi, 17
Dixippus, 7; 25
Dociostaurus, 162
Dog sucking louse. see *Linognathus setosus*
Doralis sambuci, 109
Doralis fabae, 109
Doryphora decemlineata, 157
Drepanosiphum platanoides, 76
Dried fruit beetle. see *Carpophilus hemipterus*
Drosophila, 17; 130; 136; 141; 156
Drosophila melanogaster (vinegar fly; "genetical fruit-fly"), 17; 19; 94; 101; 136; 156
Drosophila virilis, 17
Drug store beetle. see *Stegobium paniceum*
Duboisia hopwoodi (plant), 130; 131; 149
Dykraneura, 16
Dysdercus fasciatus, 3

E

Earias insulana, 17
Earworm, corn. see *Heliothis armigera*
Eastern tent caterpillar. see *Malacosoma americanum*
Eggplant flea beetle. see *Epitrix fuscula*
  lacebug. see *Gargraphia solani*
Elatrids, 2
Electrophorus (genus of fishes), 134
Elm leaf beetle. see *Galerucella xanthomelaena*
Empoasca, 2
Empoasca fabae (potato leafhopper), 13; 50; 56; 59; 130; 159; 172; 183
Encarsia formosa, 17
Enterobius vermicularis (Nemotohelminthes; human pinworm), 142; 177
Entomobrya, 96
Eomenacanthus, 130
Eomenacanthus stramineus (chicken body louse), 17; 61; 183
Eotetranychus carpini borealis, 35; 36; 54; 126
Eotetranychus yumensis, 85
Ephestia, 37; 99; 104; 122
Ephestia cautella (almond or fig worm), 169
Ephestia elutella (tobacco moth), 101; 114
Ephestia kuehniella (=kühniella) (Mediterranean flour moth), 13; 17; 28; 29; 30; 72; 76; 89; 99; 101; 104; 114; 117; 134; 138; 143; 169; 179; 184; 186
Epicauta, 11; 188
Epicauta pennsylvanica (black blister beetle), 130
Epilachna, 31; 114; 116
Epilachna corrupta, 157
Epilachna varivestis (Mexican bean beetle), 9; 10; 11; 13; 15; 17; 30; 34; 40; 46; 50; 59; 67; 77; 96; 109; 116; 120; 130; 132; 138; 139; 142; 149; 156; 157; 158; 159; 168; 170; 183; 188
Epitrix, 120
Epitrix cucumeris (potato flea beetle), 13; 25; 30; 59; 183
Epitrix fuscula (eggplant flea beetle), 25; 59
Epitrix hirtipennis (tobacco flea beetle), 30; 59; 112; 120; 183
Epitrix parvula, 130
Epitrix tuberis (tuber fleabeetle), 25
Eriophyes oleivorus, 23
Eriophyes ribi, 18
Eriophyes vitae, 132
Eriosoma americanum, 130
Eriosoma lanigerum (woolly apple aphid), 17; 49; 59; 100; 109; 129; 130; 132; 138; 141
Erythroneura comes (grape leafhopper), 16; 23; 130
Erythroneura variabilis, 17; 156
Estigmene acraea (salt-marsh caterpillar), 13; 16 30; 60; 65; 66; 67; 130; 138
Eugenia (plant genus), 170
Eulecanium corni (brown scale), 17
Eulia velutinana, 17
Eunonymus bungeanus (plant), 117; 145
Euphorbiaceae (plant family), 149
Euphorbia esula (plant), 170
Euproctis, 7; 165
Euproctis chrysorrhoea, 154; 157
European,
  corn borer. see *Pyrausta nubilalis*
  red mite. see *Paratetranychus pilosus*
  vine moth. see *Clysia ambiguella*
Eurytetranychus buxi, 17
Euschistus impictiventris (Arizona brown stink bug), 13
Euschistus tristigmus, 13; 30; 183
Eutettix, 173
Eutettix (=Circulifer) tenellus (beet leafhopper), 154
Eutrombicula, 14
Eutrombicula alfreddugesi=Trombicula irritans;=Acariscus mansoni (chiggers, jiggers, red bugs), 13; 14; 30; 73; 91; 102; 106; 110; 140
Euxoa, 7; 139; 163; 165
Euxoa segetum, 162
Evergestis rimosalis (cross-striped cabbageworm), 112; 157; 188
Eye-spotted bud moth. see *Spilonota ocellana*

F

Fagaceae (plant family), 149
Fagara macrophylla (plant), 107
Fagara xanthoxyloides (plant), 107
Fall,
  armyworm. see *Laphygma frugiperda*
  cankerworm. see *Alsophila pometaria*
  webworm. see *Hyphantria cunea*
Fannia canicularis (the little house fly), 17; 56; 61; 69; 114; 117; 120; 134; 154
Fasciolopsis buski (Platyhelminthes; Trematoda; human intestinal fluke), 177
Feltia annexa, 157
Fenusa pusilla (birch leaf-miner), 56; 59; 130
Fern scale. see *Pinnaspis aspidistrae*
Ferrisia virgata, 18

Note: The numbers following the entries indicate the Section in which the entry occurs.

Fever ticks. see *Boōphilus annulatus, Boōphilus decoloratus, Boōphilus microplus*
Fig moth. see *Ephestia cautella*
Fiorinia theae, 122
Fire ant. see *Solenopsis geminata, Wasmannia auropunctata*
Fire ant, imported. see *Solenopsis saevissima*
Firebrat. see *Thermobia domestica*
"Fire bug". see *Murgantia histrionica*
Flacourtaceae (plant family), 149; 157
Flatheaded apple tree borer. see *Chrysobothris femorata*
Flax bollworm. see *Heliothis ononis*
Flea,
  cat. see *Ctenocephalides felis*
  rat (oriental). see *Xenopsylla cheopis*
Fleabeetle,
  eggplant. see *Epitrix fuscula*
  potato. see *Epitrix cucumeris*
  tobacco. see *Epitrix hirtipennis*
Flea beetles. see *Altica ambiens, Altica bimarginata, Epitrix cucumeris, Epitrix fuscula, Epitrix hirtipennis, Phyllotreta* spp.
Fleahopper,
  cotton. see *Psallus seriatus*
  garden. see *Halticus bracteatus*
Flesh fly. see *Sarcophaga crassipalpus*
Florida red scale. see *Chrysomphalus aonidum*
Flour beetle,
  confused. see *Tribolium confusum*
  red. see *Triboleum castaneum*
Flower thrips. see *Frankliniella cephalica, Frankliniella tritici*
Fly(ies)
  black. see *Simulium* spp.
  black blow. see *Phormia regina*
  blue bottle. see *Calliphora erythrocephala, Calliphora vomitoria*
  bomb. see *Hypoderma bovis*
  bot. see *Gasterophilus*
  carrot rust. see *Psila rosae*
  domestic. see *Musca domestica*
  flesh. see *Sarcophaga crassipalpus*
  "genetical fruit". see *Drosophila melanogaster*
  greenbottle. see *Lucilia sericata, Phaenicia sericata*
  horse. see *Chrysops* spp., *Tabanus* spp.
  house. see *Musca domestica*
  human bot. see *Dermatobia hominis*
  lace-winged. see *Fannia canicularis*
  louse. see *Melophagus ovinus*
  mango. see *Anastrepha mombinpraeoptans*
  melon. see *Dacus cucurbitae*
  oriental fruit. see *Dacus dorsalis*
  stable. see *Stomoxys calcitrans*
  tsetse. see *Glossina morsitans, Glossina palpalis*
  vinegar. see *Drosophila melanogaster*
  walnut husk. see *Rhagoletis completa*
Formicidae (insect family), 50
Fowl,
  mite, northern. see *Bdellonyssus sylviarum*
  tick. see *Argas persicus*
Frankliniella, 60
Frankliniella cephalica (flower thrip), 168
Frankliniella fusca (tobacco thrips), 59
Frankliniella robusta, 20
Frankliniella tritici (flower thrips), 60; 65; 183
French bean fly. see Agromyza phaseoli
Fruit flies. see *Anastrepha, Ceratitis, Dacus, Drosophila, Rhagoletis*
Fruitfly,
  cherry. see *Rhagoletis cingulata, Rhagoletis fausta*
  "genetical". see *Drosophila melanogaster*
  Mediterranean. see *Ceratitis capitata*
  Mexican. see *Anastrepha ludens*
  oriental. see *Dacus dorsalis*
Fruit tree
  leaf roller. see *Archips argyrospila*
  red spider. see *Metatetranychus ulmi*
Fruitworm, tomato. see *Heliothis armigera*
Fuchsia (plant genus), 141
Furniture carpet beetle. see *Anthrenus vorax*

G

Galerucella xanthomelaena (elm leaf beetle), 157; 158
Galleria, 173
Galleria mellonella (wax moth), 7; 17; 78; 88; 130; 134; 138; 154
Garden,
  fleahopper. see *Halticus bracteatus*
  webworm. see *Loxostege similalis*
Gargraphia tileae, 130
Gargraphia solani (egg plant lace-bug), 59
Gasterophilus (bot flies), 13; 28
Gastrophyse cyanea, 188
Geocoris, 12; 17; 183
Geocoris punctipes, 17; 93
Geranium (plant genus), 135
German cockroach. see *Blattella germanica*
Gladiolus (plant genus), 166
Gladiolus thrips. see *Taeniothrips simplex*
Glaucoma piriformis (Protozoa), 114
Glossina, 73
Glossina morsitans (tsetse fly), 154
Glossina palpalis (tsetse fly), 17
Glover scale. see *Lepidosaphes gloverii*
Gnat, Clear Lake. see *Chaoborus astictopus*
Gnathocerus, 114
Gnorimoschema lycopersicella, 122
Gnorimoschema (=Phthorimoea) operculella (potato tuberworm), 13; 16; 42; 122
Goat louse. see *Bovicola caprae*
Golden-eye lacewing. see *Chrysopa oculata*
Goldfish. see *Carassius auratus*
Goniocotes, 130
Goniocotes gallinae, 117
Grain beetle,
  flat. see *Laemophloeus pusilla*
  saw toothed. see *Oryzaephilus surinamensis*
Grain beetles. see *Ahasverus, Laemophloeus, Oryzaephilus surinamensis*
Grain beetles, foreign. see *Ahasverus*
Grain borer, lesser. see *Rhizopertha dominica*
Grain moth, angoumois. see *Sitotraga cerealella*
Granary weevil. see *Sitophilus granarius*
Grape,
  berry moth. see *Polychrosis viteana*
  leafhopper. see *Erythroneura comes*
  mealybug. see *Pseudococcus maritimus*
  phylloxera. see *Phylloxera vitifoliae*
Graphognathus leucoloma (white-fringed-beetle). see *Pantomorus leucoloma*
Grapholitha funebrana (plum moth), 112; 130
Grapholitha (=Laspeyresia) molesta (oriental fruit moth), 16; 120; 122; 141; 158
Grasshopper,
  differential. see *Melanoplus differentialis*
  lesser migratory. see *Melanoplus mexicanus, mexicanus*
  red-legged. see *Melanoplus femur-rubrum*
  Rocky Mountain. see *Melanoplus mexicanus, mexicanus*
  two-striped. see *Melanoplus bivittatus*
Grasshoppers. see *Camnula pellucida, Melanoplus bivittatus, Melanoplus differentialis, Melanoplus femur-rubrum, Locusta* spp., *Nomadacris* spp., *Sphenarium purpurascens*
Greedy scale. see *Aspidiotus camelliae*
Green,
  chrysanthemum aphid. see *Rhopalosiphum rufomaculatum*
  citrus aphid. see *Aphis spiraecola*
  June beetle. see *Cotinis nitida*
  peach aphid. see *Myzus persicae*
Greenbottle fly. see *Lucilia sericata, Phaenicia sericata*
Greenhouse,
  leaf tier. see *Phlyctaenia rubigalis*
  orthezia. see *Orthezia insignis*
  thrips. see *Heliothrips haemorrhoidalis*
Grub,
  common cattle. see *Hypoderma lineatum*
  northern cattle. see *Hypoderma bovis*
  white. see *Phyllophaga hirticula*
Gryllodes sigillatus, 17
Gryllotalpa (mole cricket), 11
Gryllus assimilis (common black cricket), 162; 165; 181
Gryllus domesticus, 13; 134
Gulf Coast tick. see *Amblyomma maculatum*
Gypsy moth. see *Porthetria dispar, Lymantria dispar*

H

Haematobia. see *Siphona*
Haematopinus, 114
Haematopinus adventicius (hog louse), 30; 114
Haematopinus eurysternus (short-nosed cattle louse), 13; 17; 30; 61; 69; 74; 93; 117; 134; 138; 148; 167; 180; 183
Haematoxylon campechianum (plant), 149
Hairy chinch bug. see *Blissus hirtus*
Halisidota caryae, 130
Halticus bracteatus (garden fleahopper), 16
Haplophyton cimicidum (plant), 149
Haplothrips faurei, 17; 130
Harlequin bug. see *Murgantia histrionica*
Harpalus, 112
Head louse (human). see *Pediculus humanus capitis*
Heliopsis scabra (plant), 149
Heliothis, 3, 30
Heliothis armigera (corn earworm), 7; 13; 16; 17; 25; 30; 42; 56; 60; 65; 66; 67; 76; 77; 78; 98; 120; 130; 141; 146; 157; 158; 183; 188
Heliothis obsoleta (=Heliothis armigera), 76; 77; 78; 112
Heliothis ononis (flax bollworm), 17; 30; 76; 114; 130; 154
Heliothis (=Chloridea) virescens (tobacco bud worms), 16; 17; 74; 81; 117; 134; 183
Heliothis zea, 16; 17; 74; 81; 117; 134; 183
Heliothrips, 114
Heliothrips bicinctus, 26
Heliothrips fasciatus, 141
Heliothrips femoralis, 130
Heliothrips haemorrhoidalis (greenhouse thrips), 13; 17; 19; 26; 30; 59; 94; 96; 114; 117; 120; 126; 129; 132; 134; 138; 139; 183
Heliothrips simplex, 138
Heliotropum peruvianum (plant), 149
Hemiberlesia lataniae, 178
Hemisarcoptes malus, 17
Hemispherical scale. see *Saissetia hemisphaerica*
Hemitarsonemus latus (broad mite), 132; 178
Hercinothrips femoralis (banded greenhouse thrips), 17; 132
Hercothrips fumipennis (bean thrips), 18
Heterodera rostochiensis (Nematode), 45
Heteronychus sanctae-helenae (Black beetle of New South Wales), 13
Hippodamia, 12; 17; 183
Hippodamia ambigua, 101
Hippodamia convergens (convergent lady beetle), 5; 12; 17; 25; 42; 50; 56; 59; 61; 69; 81; 93; 96; 101; 112; 117; 130; 138; 139; 142; 154; 157; 167; 183
Hog. louse. see *Haematopinus adventicius*
Holly leaf miner. see *Phytomyza ilicis*
Honeybee. see *Apis mellifera*
Hop aphid (Hopvine aphid). see *Phorodon humuli*
Hoplocampa testudinea, 130
Horistonotus uhlerii (sand wireworm), 13; 30
Hornets. see *Vespula* (genus)
Horn fly. see *Siphona irritans*
Hornworm,
  tobacco. see *Protoparce sexta*
  tomato. see *Protoparce quinquemaculata*
Hornworms. see *Protoparce quinquemaculatus, Protoparce sexta*
Horse flies. see *Chrysops, Tabanus*
House,
  fly. see *Musca domestica*
  fly (little). see *Fannia canicularis*
Human,
  body louse. see *Pediculus humanus corporis*
  bot fly.. see *Dermatobia hominis*
  head louse. see *Pediculus humanus capitis*
  louse. see *Pediculus humanus*
Hyaliodes hartii, 17
Hyalopterus, 75
Hyalopterus arundinis (mealy plum aphid), 20; 114; 130
Hydaphis xylostei, 20
Hydrangea spp. (plant), 117; 132; 145; 172
Hylastinus obscurus (clover root borer), 13; 30; 56
Hylemya antiqua (onion maggot), 56; 96; 118; 158
Hylemya brassicae (cabbage maggot), 13; 30; 56; 88; 118; 120; 150; 158; 159; 183
Hylemya cilicura (seed corn maggot), 30; 56; 183
Hylemya floralis, 13; 56; 118; 120; 159
Hylemya trichodactyla, 30; 56
Hylobius radicis (pine root collar weevil), 13; 30; 150
Hymenia recurvalis (beet webworm, Australian), 188
Hypera meles, 13
Hypera postica (alfalfa weevil), 30

Note: The numbers following the entries indicate the Section in which the entry occurs.

Hyphantria cunea (Fall webworm), 7; 8; 25; 40; 112; 130
Hyphantria textor, 7; 13
Hypoderma, 69; 74
Hypoderma bovis (bombfly or northern cattle grub), 13; 74; 120; 168; 183
Hypoderma lineatum (common cattle grub), 13; 120; 168
Hyponomeuta sp., 37

I

Icerya, 138
Icerya purchasi (cottony-cushion scale), 17; 20
Illinoia *(=Macrosiphum)* pisi=*Macrosiphum onobrychis* (pea aphid), 23
Illinoia *(=Macrosiphum) solanifolii* (potato aphid), 172
Imported,
  cabbageworm. see *Pieris rapae, Ascia rapae*
  currantworm. see *Nematus ribesii*
  fire ant. see *Solenopsis saevissima*
Indian-meal moth. see *Plodia interpunctella*
Iridomyrmex humilis (Argentine ant), 30
Iris thrips. see *Bregmatothrips iridis*
Itch mite. see *Sarcoptes scabiei*
Ixodes ricinus (castor bean tick), 46; 157

J

Japanese beetle. see *Popillia japonica*
Jassid leafhoppers, 77
Jiggers. see *Acariscus mansoni, Eutrombicula alfreddugesi, Trombicula irritans*

K

Kaliofenusa ulmi (leaf-mining sawfly of the Elm), 130
Kalotermes minor (common drywood termite), 170
Ked, sheep. see *Melophagus ovinus*
Keiferia lycopersicella (tomato pinworm), 42
Kentia sp. (plant), 122
Kissing bugs. see *Triatoma* (genus)

L

Labiatae (plant family), 149
Lace-bugs. see *Corythuca*
Lace-winged flies. see *Chrysopa*
Lacewing, golden-eye. see *Chrysopa oculata*
Lachnus saligenus, 132; 134
Lady beetle,
  Australian. see *Cryptolaemus montrouzieri, Rodolia cardinalis*
  convergent. see *Hippodamia convergens*
  two-spotted. see *Adalia bipunctata*
Lady beetles. see *Adalia, Coccinella, Coleomegilla, Cryptolaemus, Cycloneda, Hippodamia, Rodolia*
Laemophloeus minutus, 37
Lantana (plant genus), 141
Laphygma, 13; 16; 30; 165
Laphygma eridania, 13
Laphygma frugiperda (Fall armyworm), 30; 139; 162; 165; 168; 183
Larch casebearer. see *Coleophora laricella*
Larder beetle. see *Dermestes lardarius*
Lasioderma serricorne (cigarette beetle or tow-bug), 1; 28; 29; 37; 88; 89; 101; 104; 114; 170; 184
Lasius, 13
Lasius americanus (=L. niger alienus americanus) (cornfield ant), 13; 30
Lasius exsectoides, 2
Lasius niger, 2
Laspeyresia (=Grapholitha) nigricana (pea moth), 13
Latania scale. see *Aspidiotus lataniae*
Latrodectus mactans (black widow spider), 30
Leafhopper,
  beet. see *Circulifer tenellus*
  blunt-nosed cranberry. see *Scleroracus vaccinii*
  cicadellid. see *Cicadellid leafhoppers*
  clover. see *Acertaogallia sanguinolenta*
Leafhopper, *(Continued)*
  corn. see Peregrinus maidis
  grape. see *Erythoneura comes*
  potato. see *Empoasca fabae*
Leafhoppers, 59. also see *Aceratogallia, Circulifer (=Eutettix), Empoasca, Erythroneura, Scleroracus*
Leafminer(s),
  Aster. see *Liriomyza flaveola*
  Birch. see *Fenusa pusilla*
  Boxwood. see *Monarthropalpus buxi*
  Holly. see *Phytomyza ilicis*
  Serpentine. see *Liriomyza pusilla*
Leaf-miner(s). see *Fenusa pusilla, Liriomyza* spp., *Phytomyza* spp., *Profenusia canadensis*
Leaf-mining sawfly of the Elm. see *Kaliofensua ulmi*
Leaf roller(s),
  Fruit tree. see *Archips argyrospila*
  Red-banded. see *Argyrotaenia velutinana*
  Strawberry. see *Ancylis comptana*
Leaf tier, greenhouse (or celery). see *Phlyctaenia rubigalis*
Leafworm, cotton. see *Alabama argillacea*
Leguminosae (plant family), 149
Leopard moth. see *Zeuzera pyrina*
Lepidoderma, 13; 28; 30
Lepidosaphes, 75
Lepidosaphes beckii (purple scale), 17
Lepidosaphes camelliae (Camellia scale), 122
Lepidosaphes gloverii (Glover scale), 122
Lepidosaphes ulmi (apple oyster-shell scale), 77; 168
Lepisma saccharina (silverfish), 50
Leptinotarsa, 17; 112; 149
Leptinotarsa decemlineata (Colorado potato beetle), 2; 7; 8; 9; 10; 11; 13; 25; 30; 40; 56; 62; 77; 78; 81; 112; 130; 132; 139; 157; 158; 168; 183
Leptothrips mali, 17; 112
Lesser,
  grain borer. see *Rhizopertha dominica*
  migratory grasshopper. see *Melanoplus mexicanus mexicanus*
Leucophaea maderae, 17; 146
Leucopis puncticornis, 59
Lice. see *Bovicola, Damalinia, Eomenacanthus, Goniocotes, Haematopinus, Linognathus, Lipeurus, Menopon, Pediculus, Phthirus, Solenopotes*
Ligustrum obtusifolium (plant), 117; 145
Lilac borer. see *Podosesia syringae syringae*
Liliaceae (plant family), 149
Lilium longiflorum (plant), 132
Lily aphid, crescent marked. see *Myzus circumflexus*
Limonius, 23; 56; 82; 88; 124
Limonius californicus, 4; 28; 37; 45; 51; 82; 87; 88; 90; 104; 122; 124; 150; 186; 188
Limonius canus (Pacific Coast wireworm), 4; 28; 37; 51; 82; 88; 104; 114; 122; 124; 150; 186; 188
Linognathus setosus (dog sucking louse), 13
Linognathus (=Haematopinus) vituli (short-nosed cattle louse), 30
Linum usitatissimum (plant), 170
Lipeurus, 130
Liponyssus (=Bdellonyssus) bacoti (tropical rat mite), 34
Liriomyza, 17
Liriomyza flaveola (aster leafminer), 30; 138
Liriomyza orbona (pea leaf miner), 13; 16; 30; 112; 132
Liriomyza (=Agromyza) pusilla (serpentine leaf miner), 30; 60
Listroderes costirostris obliquus (vegetable weevil), 96
Listroderes obliquus, 17
Lithocolletis, 130
Little,
  carpenterworm. see *Prionoxystus macmurtrei*
  house fly (the). see *Fannia canicularis*
Locust, seventeen year. see *Cicada (=Magicicada) septendecim*. also see *Periodical cicada*
Locusta, 7; 8; 94; 139; 162; 163
Locusta migratoria, 7; 13; 27; 76; 78; 134; 163
Locusta migratoria migratorioides, 17; 30; 76; 114; 125; 134; 139; 154; 162; 179; 183
Lonchocarpus (plant genus), 157
Lonchocarpus urucu (plant), 157
Lonchocarpus utilis (plant), 157
Lone-star tick. see *Amblyomma americanum*
Long-tailed mealybug. see *Pseudococcus adonidum*
Lonicera (plant genus), 117; 145
Louse,
  bird. see *Mallophaga*
  body. see *Pediculus humanus corporis*
  cattle biting. (or little red) see *Bovicola bovis*
  cattle sucking. see *Solenoptes capillatus*
  chicken body. see *Eomenacanthus stramineus*
  common body. (poultry) see *Menopon gallinae*
  crab. see *Phthirus pubis*
  dog sucking. see *Linognathus setosus*
  goat. see *Bovicola caprae*
  head. (human) see *Pediculus humanus capitis*
  hog. see *Haematopinus adventicius*
  human. see *Pediculus humanus corporis, P. humanus capitis*
  pubic. see *Phthirus pubis*
  shaft. see *Menopon gallinae*
  short-nosed cattle. see *Haematopinus eurysternus*
Louse fly (sheep). see *Melophagus ovinus*
Loxostege, 50
Loxostege similalis (garden webworm), 25; 183
Loxostege sticticalis (beet webworm), 154
Lucilia, 82; 142
Lucilia cuprina (blow fly maggot of sheep, Australian), 13
Lucilia (=Phaenicia) sericata (greenbottle fly), 17; 114; 118; 130; 134; 142
Ludius, 13
Ludius aeripennis, 30
Lycophotia (=Peridroma) margaritosa (variegated cutworm), 168
Lycophotia margaritosa saucia, 130
Lycoria inconstans, 17
Lyctid beetles, 140
Lyctus (powder post beetles), 104; 140; 168
Lygaeus kalmii, 5; 76; 77; 130
Lygaeus mendax, 23
Lygidea mendax (apple redbug), 130
Lygus, 13; 17; 50; 56; 159
Lygus atriflavus, 154; 157
Lygus campestris, 130; 168
Lygus elisus, 154; 157
Lygus hesperus, 154; 156; 157
Lygus oblineatus (tarnished plant bug), 13; 30; 159
Lygus pratensis (tarnished plant bug), 130; 168
Lymantria (genus; tussock moths), 173
Lymantria dispar (gypsy moth), 25; 94; 112; 165
Lymantria monacha (nun moth), 76; 78; 154; 157; 173

M

Macrocentrus, 173
Macrocentrus ancylovorus, 17; 158
Macrodactylus subspinosus (rose chafer), 112; 154
Macrosiphoniella sanborni (chrysanthemum aphid), 13; 17; 19; 20; 26; 59; 111; 130; 132; 135; 157; 166
Macrosiphum, 114
Macrosiphum euphorbiae, 18; 132; 134; 172; 179
Macrosiphum gei, 18; 26; 132; 172
Macrosiphum lineatum, 26
Macrosiphum onobrychis, 23; 130; 138
Macrosiphum pisi (pea aphid), 2; 16; 17; 20; 23; 30; 56; 59; 67; 93; 109; 114; 120; 130; 132; 134; 138; 157; 168; 179; 183; 188
Macrosiphum rosae (rose aphid), 18; 20; 59; 130; 132; 172
Macrosiphum sanborni, 141; 172
Macrosiphum solanifolii (potato aphid), 3; 17; 59; 130; 132; 138; 154
Maggot,
  apple. see *Rhagoletis pomonella*
  cabbage. see *Hylemya brassicae*
  onion. see *Hylemya antiqua*
  seed-corn. see *Hylemya cilicrura*
Magnolia glauca (plant), 145
Malacosoma americanum (=M. americana) (eastern tent caterpillar), 7; 8; 10; 13; 112; 130; 141; 157; 168; 183
Mallophaga, 163
Malus sp. (plant), 145
Mamestra picta, 130
Mammaea americana (plant), 149
Mange mites. see *Psoroptes bovis, Sarcoptes scabiei*
Mango fly. see *Anastrepha mombinpraeoptans*
Masonaphis rhododendri, 18
May bettle. see *Melolontha vulgaris*

Note: The numbers following the entries indicate the Section in which the entry occurs.

Meadow spittlebug. see *Philaenus leucophthalmus*
Mealworm,
  dark. see *Tenebrio obscurus*
  yellow. see *Tenebrio molitor*
Mealworms. see *Tenebrio* spp.
Mealybug,
  citrophilus. see *Pseudococcus gahani*
  citrus. see *Pseudococcus citri*
  Comstock. see *Pseudococcus comstocki*
  grape. see *Pseudococcus maritimus*
  long-tailed. see *Pseudococcus adonidum*
  Mexican. see *Phenacoccus gossypii*
  pineapple. see *Pseudococcus brevipes*
Mealybugs. see *Pseudococcus, Phenacoccus, Orthezia*
Mealy plum aphid. see *Hyalopterus arundinis*
Medicago sativa (plant), 170
Mediterranean,
  flour moth. see *Ephestia kühniella*
  fruit fly. see *Ceratitis capitata*
Melanoplus, 13; 30; 114; 130; 157; 169; 183
Melanoplus bivittatus (two-striped grasshopper), 2; 7; 8; 56; 94; 142; 162; 163
Melanoplus differentialis (differential grasshopper), 2; 7; 8; 13; 17; 25; 30; 41; 56; 76; 94; 96; 100 112; 114; 134; 138; 157; 162; 163; 165; 179; 183
Melanoplus femur-rubrum (red-legged grasshopper), 7; 8; 13; 17; 77; 78; 94; 96; 154; 157; 159
Melanoplus leukinus, 2
Melanoplus mexicanus mexicanus (lesser migratory grasshopper, also Rocky Mountain grasshopper), 2; 30; 56; 76; 162; 183
Melanthium virginicum (plant), 149
Melia azedarach (plant), 149
Meliaceae (plant family), 149
Meligethes aeneus, 13
Melilotus (plant genus), 170
Melittia satyriniformis (squash borer), 25; 30; 56; 112; 114; 130; 138
Meloidogyne halpa (Nematode), 59
Melolontha, 154, 157
Melolontha melolontha, 2; 30; 56; 143; 183
Melolontha vulgaris (May beetle), 13; 28; 49
Melon,
  aphid. see *Aphis gossypii*
  fly. see *Dacus cucurbitae*
  worm. see *Diaphania hyalinata*
Melonotus, 30; 114
Melophagus, 173
Melophagus ovinus (sheep-tick, louse fly or ked), 16; 30; 96; 114; 120; 157
Menopon, 130
Menopon biseriatum, 129
Menopon gallinae=M. pallidum (shaft louse, small body louse, common body louse of poultry), 117
Metaphycus helvolus, 168
Metaphycus luceolus, 17; 138
Metasyrphis wiedemannii, 59
Metatetranychus citri, 17; 132; 134
Metatetranychus ulmi (fruit tree red spider), 10; 14; 15; 17; 24; 31; 33; 34; 35; 36; 54; 59; 61; 62; 63; 64; 80; 83; 85; 126; 136; 138
Mexican,
  bean beetle. see *Epilachna varivestis*
  fruit fly. see *Anastrepha ludens*
  mealy bug. see *Phenacoccus gossypii*
Milkweed bug. see *Oncopeltus fasciatus*
Millettia (plant genus), 157
Millettia pachycarpa (plant), 149
Millipedes, 129
Mineola vaccinii (cranberry fruitworm), 42; 158
Mirids, 13
Mite,
  broad. see *Hemitarsonemus latus*
  bulb. see *Rhizoglyphus echinopus*
  cattle follicle. see *Demodex bovis*
  cattle mange. see *Psoroptes bovis*
  chicken. see *Dermanyssus gallinae*
  citrus bud. see *Aceria sheldoni*
  citrus red. see *Paratetranychus citri*
  citrus rust. see *Phyllocoptruta oleivora*
  clover. see *Bryobia praetiosa*
  cyclamen. see *Tarsonemus pallidus*
  desert. see *Septanychus desertorum*
  European red. see *Paratetranychus pilosus*
  itch. see *Sarcoptes scabiei*
  northern fowl. see *Bdellonyssus sylviarum*
  Pacific. see *Tetranychus pacificus*
  poultry. see *Dermanyssus gallinae*
  Schoene's. see *Tetranychus schoenei*
  tropical rat. see *Bdellonyssus bacoti*
Mite(s),
  mange. see *Psoroptes bovis, Sarcoptes scabiei, S. scabiei suis*
  spider. see Spider mite(s)
Mites (phytophagous). see *Bryobia, Eotetranychus, Eurytetranychus, Hemitarsonemus, Heteronychus, Metatetranychus, Oligonychus, Paratetranychus, Petrobia, Phyllocoptruta, Septanychus, Tarsonemus, Tetranychus*
Mole cricket(s). see *Gryllotalpa, Scapteriscus*
Monarthropalpus buxi (boxwood leaf miner), 13; 56; 130; 183
Monomorium pharaonis (pharaoh ant), 30; 181
Mordestelinus, 122
Mormon cricket. see *Anabrus simplex, Nemobius fasciatus*
Mosquito,
  common malaria. see *Anopheles quadrimaculatus*
  northern house. see *Culex pipiens*
  saltmarsh. see *Aëdes sollicitans*
  southern house. see *Culex quinquefasciatus*
  yellow fever. see *Aëdes aëgypti*
Mosquito larvae (various), 56; 70; 128; 154
Mosquitoes, 103. also see *Aedes* spp., *Anopheles* spp., *Culex* spp., *Mansonia* spp., *Theobaldi* spp.
Moth,
  almond. see *Ephestia cautella*
  Angoumois grain. see *Sitrotraga cerealella*
  Catalpa sphinx. see *Ceratomia catalpae*
  clothes. see Moth(s), clothes
  codling. see *Carpocapsa pomonella*
  diamondback. see *Plutella maculipennis*
  eye-spotted bud. see *Spilonota ocellana*
  fig. see *Ephestia cautella*
  grape berry. see *Polychrosis viteana*
  gypsy. see *Porthetria (=Lymantria) dispar*
  Indian meal. see *Plodia interpunctella*
  leopard. see *Zeuzera pyrina*
  Mediterranean flour. see *Ephestia küehniella*
  nun. see *Lymantria monacha*
  oriental. fruit see *Grapholitha molesta*
  pea. see *Laspeyresia nigricana*
  plum. see *Grapholitha funebrana*
  satin. see *Stilpnotia salicis*
  tobacco. see *Ephestia elutella*
  tussock. see Moth(s), tussock
  wax. see *Galleria mellonella*
Moth(s),
  clothes. see *Tinea pellionella, Tineola bisselliella, Trichophaga tapetzella*
  tussock. see *Lymantria* spp.
Mountain pine beetle. see *Dendroctonus monticolae*
Mundulea (plant genus), 157
Mundulea sericea (=suberosa) (plant), 149
Murgantia, 183
Murgantia histrionica (harlequin bug, "firebug", "calico back"), 46; 157
Musa sp. (plant), 122
Musca, 31; 73; 103; 104; 114; 132; 134; 135; 136; 149; 156; 157; 171; 180
Musca domestica (house fly), 1; 2; 3; 6; 7; 8; 10; 13; 16; 17; 18; 19; 21; 22; 23; 27; 30; 37; 43; 46; 49; 50; 54; 56; 57; 61; 62; 67; 69; 70; 71; 72; 74; 81; 87; 93; 95; 96; 100; 106; 107; 108; 109; 110; 117; 120; 125; 129; 130; 132; 133; 134; 135; 136; 137; 138; 141; 142; 143; 146; 147; 148; 153; 154; 156; 157; 158; 159; 160; 162; 165; 170; 171; 173; 176; 178; 179; 180; 182; 183; 184; 187; 188
Musca domestica, various strains or biotypes susceptible to (non-R or S) or resistant to (R) various insecticides,
  Auburn strain, 30; 61; 69; 70; 96; 120; 159
  Ballard strain, 2; 17; 30; 56; 114; 156
  Bellflower strain, 2; 3; 16; 17; 96; 114; 120; 147; 154; 156; 183
  Bruce-Decker Lindane-R biotype, 156
  Biotype K, 136; 156
  "Campus" (DDT-R) biotype, 117; 134; 156; 173
  Chlordane-R biotype, 156
  Chlordane-I biotype, 17; 114; 156
  CSMA biotype (DDT non-R), 187
  DDD-R biotype, 147; 156
  DDT-I biotype, 17; 114; 120; 137; 146; 154; 156; 183
  DDT-III biotype, 17; 114; 120; 146; 154; 156
  DDT non-R biotype(s), 56; 96; 114; 117; 120; 146; 147; 153; 154; 156; 171; 173; 183; 187
  DDT-R biotype(s), 61; 69; 114; 117; 120; 134; 146; 147; 154; 156; 171; 173; 180; 183; 187
  DDT-S biotypes, 2; 3; 56; 61; 146; 154; 156; 171; 183
Musca domestica, various strains or biotypes susceptible to (non-R or S) or resistant to (R) various insecticides, *(Continued)*
  DDT-W biotype, 17; 114; 120; 146; 154; 156; 183
  DDT non-R biotype(s), 16; 154; 156
  Dieldrin-I biotype, 17; 114; 156
  Ellenville (DDT-R) biotype, 138; 156
  F 151 biotype, 138; 156
  Fünen 151 biotype (=F 151), 156
  J-74 biotype, 138; 156
  J-79 biotype, 138; 156
  Jutland 74 biotype (=J 74), 156
  Jutland 79 biotype (=J 79), 156
  "KUN" (DDT-non R) biotype, 117; 134; 156; 173
  Lab-I (=Laboratory) strain (DDT-non R, DDT-S biotypes), 114; 120; 137; 146; 154; 156; 183
  Lab-II (=Laboratory) strain (DDT-non R, DDT-S biotype), 114; 120; 137; 146; 154; 156; 183
  Laboratory strain, 17; 114; 120; 154; 156; 183
  Laboratory 9 and 17 biotypes, 156
  Laton strain, 17; 156
  LDD strain, 2; 17; 30; 56; 114; 156
  Lindane-I biotype, 17; 114; 146; 154; 156; 183
  Lindane-R biotypes, 114; 156; 183
  Methoxy-I biotype, 17; 114; 120; 137; 146; 154; 156; 183
  Methoxychlor-R biotype, 147; 156; 183
  Multi-I biotype, 17; 114; 120; 137; 146; 154; 156; 183
  Multi-II biotype, 17; 114; 120; 156
  Multi-III biotype, 17; 114; 120; 146; 154; 156
  Multi-IV biotype, 17; 114; 120; 156
  Multi-R biotype(s), 183
  NAIDM strain, 17; 71; 74; 120; 146; 156
  Non-R biotype(s), 17; 156
  Ontario strain, 17; 96; 114; 120; 154; 156; 183
  Orlando-Beltsville (DDT-R) biotype, 71; 74; 156; 187
  Orlando strain, 30; 61; 69; 70; 96; 120; 156
  Orlando #1 strain, 2; 17; 30; 56; 114; 156
  Orlando Special biotype, 17; 156
  Para-Oxon strain, 137; 156
  Para-Oxon-I strain, 137; 156
  Pollard strain, 2; 16; 96; 114; 120; 154; 156; 183
  Pyro-I (Pyrethrin-I) biotype, 17; 114; 146; 154; 156
  Riverside strain, 17; 96; 114; 120; 154; 156; 183
  San José strain, 17; 96; 114; 120; 154; 156; 183
  Stauffer strain, 17; 156
  Super-Laton strain, 17; 147; 156
  Swiss strain K, 136; 156
  Toxaphene® -R biotype, 156; 183
  Toxaphene® -I biotype, 156
  Univ. of Indiana biotype, 146
  Z 98 biotype, 138
  Z 127 biotype, 138
  Z 149 biotype, 138
  Zealand 98 biotype, 156
  Zealand 127 biotype, 156
  Zealand 129 biotype, 156
  Zealand 149 biotype, 156
  Zealand 150 biotype, 156
Musca vicina, 114
Muscina stabulans, 129
Mycoptes musculinus, 54
Mylabris pisorum. see *Bruchus pisorum*
Myrtaceae (plant family), 149
Myzocallis tiliae, 76
Myzodes persicae, 109
Myzus, 75
Myzus ascalonicus, 18
Myzus cerasi, 59; 125; 132
Myzus circumflexus (crescent-marked lily aphid), 20; 26
Myzus convolvuli, 132
Myzus persicae (green peach aphid), 17; 18; 20; 26; 59; 100; 111; 114; 117; 130; 132; 134; 138; 154; 156; 157; 159; 172; 179
Myzus porosus, 100; 130; 134; 179
Myzus solanifolii, 130

N

Nabis, 17
Nabis ferus (a damsel bug), 17; 93; 183
Nasturtium (plant genus), 138; 170
Necator americanus (Nematohelminthes; American hookworm), 177
Necrobia, 114

Note: The numbers following the entries indicate the Section in which the entry occurs.

Necrobia rufipes (red-legged ham beetle), 89
Nematus (=Pteronidea) ribesii (imported currantworm), 25
Nemobius fasciatus (Mormon cricket), 162
Neomyzaphis abietina, 132
Nezara, 30; 183
Nezara viridula (southern green stink bug), 13; 46; 157; 159
Nicandra physalodes (plant), 149
Nicotiana (plant genus), 130
Nicotiana spp. (plants), 149
Nicotiana glauca (plant), 149
Nicotiana rustica (plant), 130
Nicotiana sylvestris (plant), 131
Nicotiana tabacum (plant), 130; 131; 149
Niptus, 114
Noctuidae (insect family), 50
Nomadacris, 76
Northern,
  cattle grub. see *Hypoderma bovis*
  fowl mite. see *Bdellonyssus sylviarum*
  house mosquito. see *Culex pipiens*
Nun moth. see *Lymantria monacha*

O

Ocimum basilicum (plant), 149
Odontria, 37
Oligonychus ununguis, 17
Oligonychus yothersi, 17
Olive scale. see *Parlatoria oleae*
Oncopeltus, 1; 3; 31; 134; 158
Oncopeltus fasciatus (milkweed bug), 2; 3; 5; 7; 13; 17; 19; 23; 30; 56; 76; 77; 81; 88; 94; 96; 104; 108; 117; 130; 132; 134; 135; 138; 154; 157; 158; 159; 171; 183; 188
Onion,
  maggot. see *Hylemya antiqua*
  thrips. see *Thrips tabaci*
Oniscidae (Sowbugs, pillbugs) (arthropod family), 17
Operophthera brumata (winter moth), 76; 100; 134; 137; 138; 141
Opius, 17
Opius oöphilus, 17
Orange tortrix. see *Argyrotaenia citrana*
Orchidophilus, 122
Oriental,
  beetle. see *Anomala orientalis*
  cockroach. see *Blatta orientalis*
  fruit fly. see *Dacus dorsalis*
  fruit moth. see *Grapholitha molesta*
  rat flea. see *Xenopsylla cheopis*
Orius, 12; 17; 183
Orius tristicolor, 17
Ornithodoros megnini (spinose ear-tick, Texas Mexico), 13
Orinthodoros moubata, 13; 154; 157
Orthezia insignis (greenhouse orthezia), 130
Oryctes nasicornis (rhinoceros beetle), 154; 157
Oryzaephilus, 76; 99; 122
Oryzaephilus surinamensis (saw-toothed grain beetle), 1; 3; 13; 16; 17; 19; 28; 29; 37; 46; 52; 86; 87; 88; 89; 101; 104; 114; 120; 122; 154; 157; 169; 170; 182; 184
Oryza sativa (plant), 170
Osmia rufa, 13; 17
Oxydendrum arboreum (plant), 117; 145

P

Pachyrhizus erosus (plant), 149
Pachysema, 17
Pachyzancla bipunctalis, 13
Pacific,
  Coast wireworm. see *Limonius canus*
  mite. see *Tetranychus pacificus*
Painted lady. see *Vanessa cardui;* also see *Cynthia (=Vanessa) cardui*
Pale western cutworm. see *Agrotis orthogonia*
Paleacrita vernata (Spring cankerworm), 50
Palm or Dictyospermum scale. see *Chrysomphalus dictyospermi*
Panicum mileaceum (plant), 170
Pantomorus, 122
Pantomorus (=Graphognathus) leucolma (white-fringed beetle), 13; 25; 120
Paper nest wasps. see *Polistes*
Paratetranychus, 143
Paratetranychus citri (citrus red mite), 5; 13; 15; 24; 31; 35; 36; 53; 54; 59; 76; 77; 78; 80; 94; 96; 114; 117; 126; 130; 132; 134; 138
Paratetranychus ilicis, 10; 59; 122
Paratetranychus pilosus (European red mite), 14; 24; 31; 53; 54; 55; 59; 62; 83; 85; 126; 138; 141
Paratetranychus pratensis, 35; 53; 54; 59; 85; 126
Paratetranychus ununguis (spruce spider mite), 55; 59; 77
Paratetranychus yothersi, 93
Paratrioza cockerelli (potato psyllid, potato psylla), 168
Parlatoria, 138
Parlatoria oleae (olive scale), 138
Parthenocissus quinquefolia (plant), 149
Parthenothrips dracenae, 26
Passalus, 94; 163
Pea,
  aphid. see *Illinoia pisi, Macrosiphum pisi, Macrosiphum onobrychis*
  leaf miner. see *Liriomyza orbona*
  moth. see *Laspeyresia nigricana*
  weevil. see *Bruchus pisorum*
Peach,
  silver mite. see *Vasates cornutus*
  tree borer. see *Aegeria (=Sanninoidea* or *Conopia) exitiosa*
  twig borer. see *Anarsia lineatella*
Pear thrips. see *Taeniothrips inconsequens*
Pectinophora gossypiella (pink bollworm), 14; 42; 120; 158
Pedaliaceae (plant family), 149
Pediculus, 17; 23; 134; 149; 154; 156; 171
Pediculus, DDT-R biotypes, 134
Pediculus humanus (human louse), 19; 23; 129; 135;
Pediculus humanus capitis=P. humanus humanus (human head louse), 14; 23; 156
Pediculus humanus corporis (human body louse), 13; 14; 16; 17; 19; 23; 33; 43; 62; 73; 91; 95; 96; 106; 111; 114; 117; 120; 128; 134; 140; 148; 154; 156; 171; 182
P. humanus corporis, Korean (DDT-R) biotype, 156
Pelargonium (plant genus), 141
Pemphigus auriculae (primrose aphid), 20; 132
Pemphigus betae (sugarbeet root aphid), 132
Pentalonia, 100; 130
Pentatrichopus fragaefolii, 132; 172
Pepper weevil. see *Anthonomus eugenii*
Peregrinus maidis (corn leafhopper), 59; 132; 134
Peridroma (=Lycophotia) margaritosa (variegated cutworm), 13; 168
Periodical cicada. see *Cicada septendecim*
Periplaneta, 114; 137; 147; 149; 156; 163
Periplaneta americana (American cockroach), 2; 3; 7; 10; 13; 16; 17; 18; 21; 23; 27; 30; 34; 44; 48; 49; 50; 51; 56; 57; 61; 69; 71; 73; 74; 75; 76; 77; 78; 93; 94; 95; 96; 103; 106; 109; 110; 111; 112; 114; 117; 120; 125; 129; 130; 132; 134; 135; 137; 138; 142; 143; 144; 146; 147; 154; 157; 158; 159; 161; 162; 163; 167; 168; 170; 179; 182; 183; 187
Petrobia latens, 54; 59; 85; 93; 126
Petrobia tritici, 168
Phaedon, 172
Phaedon cochleariae, 3; 13; 132; 137; 154; 164
Phaenicia (=Lucilia) sericata (greenbottle fly), 17
Pharaoh ant. see *Monomorium pharaonis*
Phaseolus limensis (plant), 170
Phaseolus vulgaris (plant), 170
Phellodendron amurense (plant), 149
Phenacoccus, 141
Phenacoccus gossypii (Mexican mealybug), 26; 130; 132; 178
Philaenus leucophthalmus (meadow spittlebug), 13; 30; 100; 130; 183
Phlegethontius, 7
Phlogophera meticulosa, 112
Phlyctaenia rubigalis (=P. ferrugalis) (greenhouse or celery leaf tier), 10; 13; 130; 134; 188
Phoenix sp. (plant), 122
Phormia, 73; 142
Phormia regina (black blow fly), 17; 114; 130; 132; 134; 142; 154
Phorodon humuli (hop aphid), 20; 59; 100; 132; 138; 172
Phoxinus phoxinus (fish), 162
Phryganidia californica, 17; 96
Phthirus pubis (crab or pubic louse), 14; 23; 111
Phyllaphis fagi, 76
Phyllocoptruta oleivora (citrus rust mite), 15; 17; 85
Phyllodecta, 132
Phyllophaga hirticula (white grub), 51
Phyllotreta, 17
Phylloxera (grape), 18; 28
Phylloxera (root), 132
Phylloxera vastatrix, 61; 63; 109
Phylloxera vitifoliae (grape phylloxera), 17; 28; 141
Physalis mollis (plant), 149
Phytomyza atricornis, 20
Phytomyza ilicis (holly leaf miner), 56; 59
Phytonomus, 13
Pickleworm. see *Diaphania nitidalis*
Pieris, 13; 17; 132; 164; 172
Pieris brassicae, 5; 137; 154; 162; 164; 165; 168; 172
Pieris (=Ascia) rapae (imported cabbageworm), 3; 7; 13; 16; 25; 30; 77; 78; 94; 112; 114; 120; 130; 139; 156; 158; 159; 183; 188. also see *Ascia rapae*
Pigeon tremex. see *Tremex columba*
Pill bug(s). see *Armadillidium nosatum*
Pilophorus perplexus, 17
Pimenta racemosa (plant), 149
Pimephales promelas (fish), 183
Pine,
  root collar weevil. see *Hylobius radicis*
  tick moth. see *Rhyacionia frustrana*
Pineapple mealybug. see *Pseudococcus brevipes*
Pink bollworm. see *Pectinophora gossypiella*
Pinnaspis, 138
Pinnaspis (=Hemichionaspis) aspidistrae (fern scale), 178
Pinus strobus (plant), 117; 145
Pinworm, tomato. see *Keiferia lycopersicella*
Piper nigrum (plant), 146; 147
Plagiognathus obscurus, 17
Planococcus citri, 17
Plant bug,
  rapid. see *Adelphocoris rapidus*
  tarnished. see *Lygus oblineatus*
Platysymia cecropiae, 158
Pliophila casei, 154
Plodia, 99; 122
Plodia interpunctella (Indian-meal moth), 28; 29; 37; 89; 104; 121; 122
Plum,
  aphid, mealy. see *Hyalopterus arundinis*
  curculio. see *Conotrachelus nenuphar*
  moth. see *Grapholitha funebrana*
Plusia gamma, 72; 132; 138; 143
Plutella, 173
Plutella maculipennis (diamond-back moth), 3; 25; 80; 112; 130; 134; 154; 179; 188
Podosesia syringae fraxini (ash tree borer), 28
Podosesia syringae syringae (lilac borer), 28
Pogonomyrmex barbatus (red harvester ant), 17; 30; 96
Poinsettia (plant genus), 138; 170; 179
Polistes (paper nest wasps), 13
Polycelis nigra (Platyhelminth), 21; 161
Polychrosis viteana (grape berry moth), 13; 112; 138; 183
Polygonia interrogationis, 112
Polyphylla perversa, 87
Popillia japonica (Japanese beetle), 2; 7; 8; 9; 13; 17; 23; 28; 30; 87; 88; 89; 96; 112; 116; 122; 129; 130; 134; 135; 138; 142; 149; 154; 157; 158; 161; 183; 188
Populus sp. (plant), 117; 145
Porthetria (=Lymantria) dispar (gypsy moth), 17; 154; 157; 162
Potato,
  aphid. see *Illinoia solanifolii, Macrosiphum solanifolii*
  flea beetle. see *Epitrix cucumeris*
  leafhopper. see *Empoasca fabae*
  psylla. see *Paratrioza cockerelli*
  psyllid. see *Paratrioza cockerelli*
  tuberworm. see *Gnorimoschema operculella*
Poultry mite. see *Dermanyssus gallinae*
Powder post beetles. see *Lyctus, Ptinus*
Primrose aphis. see *Pemphigus auriculae*
Primula (plant genus), 184
Prionoxystus macmurtrei (little carpenterworm), 28; 130
Prionoxystus robiniae (carpenterworm), 28; 130
Processional caterpillar. see *Thaumetopoea processionaria*
Prodenia, 11; 16; 30; 94; 142; 163; 165; 173
Prodenia eridania (southern armyworm), 7; 8; 13; 17; 30; 40; 42; 50; 94; 96; 109; 112; 114; 130;

Note: The numbers following the entries indicate the Section in which the entry occurs.

Prodenia eridania (southern armyworm), *(Continued)*
  139; 154; 157; 162; 168; 170; 173; 183
Prodenia litura, 2; 42; 56; 112
Profenusia canadensis (cherry leafminer), 13; 30
Prospattella aurantii, 17
Protoparce, 112
Protoparce quinquemaculata (tobacco hornworm), 16; 25; 130; 183
Protoparce sexta (tobacco hornworm), 2; 16; 17; 25; 40; 42; 56; 81; 96; 108; 114; 117; 130; 134; 138; 139; 154; 183
Psallus seriatus (cotton fleahopper), 13; 23; 30; 60; 65; 66; 134; 183
Pseudaletia unipuncta, 188
Pseudhomalpoda prima, 17
Pseudoaphycus, 17
Pseudococcus, 138
Pseudococcus adonidum (=Pseudococcus longispinus) (long-tailed mealybug), 17; 138; 178
Pseudococcus brevipes (pineapple mealybug), 172
Pseudococcus citri (citrus mealybug), 18; 23; 26; 59; 135; 138; 141; 157; 178
Pseudococcus comstocki (Comstock mealybug), 138; 141; 183
Pseudococcus gahani (citrophilus mealybug), 138
Pseudococcus kenyae, 18
Pseudococcus maritimus (grape mealybug), 13; 17; 23; 26; 30; 122; 138; 178
Pseudococcus njalensis, 18
Psila rosae (carrot rust fly), 129
Psoroptes bovis (cattle mange mite), 113
Psychoda (insect family), 17
Psylla, 143; 166
Psylla,
  pear. see *Psylla pyri, Psylla pyricola*
  potato. see *Paratrioza cockerelli*
  rose. see *Psylla rosae*
Psylla pyricola (pear psylla), 13; 30; 75; 100; 130; 138; 183
Psylla pyri (pear psylla), 13; 138; 179
Psylla (=Psyllia) pyricola (pear psylla), 13; 30; 75; 100; 130; 138; 183
Psylla (=Psyllia) rosae (rose psylla), 13
Pterandrus, 42; 165
Pteronus ribesii (currant sawfly), 5
Ptinus, 114
Ptinus tectus (one of the powder post beetles), 184
Public louse. see *Phthirus pubis*
Purple scale. see *Lepidosaphes beckii*
Pyrausta nubilalis (European corn borer), 2; 17; 19; 30; 33; 56; 93; 96; 120; 130; 138; 150; 158; 188
Pyracantha (plant genus), 170
Pyrrochoris apterus, 132; 134

Q

Quercus borealis (plant), 145
Quercus palustris (plant), 117; 145

R

Ranunculaceae (plant family), 149
Rana pipiens (amphibian; grass frog), 158
Raphanus sativus (plant), 170
Rapid plant bug. see *Adelphocoris rapidus*
Rat flea, oriental. see *Xenopsylla cheopis*
Red,
  banded leaf roller. see *Argyrotaenia*
  bug, apple. see *Lygidea mendax*
  bug(s). see *Acariscus mansoni, Eutrombicula alfreddugesi, Trombicula irritans*
  flour beetle. see *Tribolium castaneum*
  harvester ant. see *Pogonomyrmex barbatus*
  legged grasshopper. see *Melanoplus femurrubrum*
  spider mites. see *Paratetranychus citri, Tetranychus sexmaculatus, Tetranychus lewisi*
Reticulotermes, 140
Reticulotermes flavipes, 42; 130; 142; 165; 174
Rhagoletis, 138
Rhagoletis cingulata (cherry fruit fly), 7; 40; 120; 130; 138
Rhagoletis completa (walnut husk fly), 2; 17; 42; 96; 120; 134
Rhagoletis fausta (cherry fruit fly), 7; 25; 130
Rhagoletis pomonella (apple maggot), 7; 17; 25; 50; 130
Rhinoceros beetle. see *Oryctes nasicornis*
Rhipicephalus appendiculatus, 13
Rhizoecus terrestis, 22
Rhizoglyphus echinopus (bulb mite), 59
Rhizopertha (=Rhyzopertha), 99
Rhizopertha (=Rhyzopertha) dominica (lesser grain borer), 1; 13; 28; 29; 37; 52; 69; 86; 87; 88; 89; 101; 104; 114; 117; 121; 122; 170
Rhodnius, 130; 154; 157
Rhodnius prolixus (assassin bug), 154
Rhopalosiphoninum latysiphon, 18
Rhopalosiphum prunifoliae (apple-grain aphid), 71; 130
Rhopalosiphum pseudobrassicae (turnip aphid), 59; 114; 130; 138; 157; 172
Rhopalosiphum rufomaculatum (green chrysanthemum aphid), 17; 132; 138; 141
Rhopobota naevana, 17
Rhyacionia frustrana (pine tick moth), 130
Rice weevil. see *Sitophilus oryzae*
Ricinus communis (plant), 149
Rocky Mountain wood tick. see *Dermacentor andersoni*
Rodolia cardinalis (Australian lady beetle or vedalia), 17
Rootworm,
  corn. see *Diabrotica longicornis*
  corn (western). see *Diabrotica virgifera*
Rose,
  aphid. see *Macrosiphum rosae*
  chafer. see *Macrodactylus subspinosus*
Roundheaded apple tree borer. see *Saperda candida*
Rumex acetosella (plant), 170
Rutaceae (plant family), 149
Ryania speciosa (plant), 149; 157

S

Sabadilla officinarum (plant). see *Schoenocaulon officinale*
Saint Paulia (=Saintpaulia) (plant), 132; 138
Saissetia hemisphaerica (hemispherical scale), 138; 178
Saissetia oleae (black scale), 20; 87; 89; 101; 130; 178
Saissetia oleae, Methyl bromide-R strain, 122
Salix sp., (plant), 117; 145
Salmo gairdneri shasta (fish), 162
Salt-marsh,
  caterpillar. see *Estigmene acraea*
  mosquito. see *Aëdes sollicitans*
Salvia (plant genus), 135
Salvia officinalis (plant), 149
Sand wireworm. see *Horistonotus uhleri*
San José scale. see *Aspidiotus perniciosus*
Sanninoidea (=Aegeria; Canopia) exitiosa (peach tree borer), 49; 88; 138; 150
Saperda candida (roundheaded apple tree borer), 26
Sapindaceae (plant family), 149
Sapindus marginatus (plant), 149
Sapphaphis plantaginea, 61; 63; 109; 132
Sapphaphis pyri, 109
Sarcophaga crassipalpus (a flesh fly), 154
Sarcoptes scabiei (itch mite, mange mite, sarcoptic mange), 13; 14; 117; 168
Sarcoptes scabiei suis (hog mange mite), 13
Sarcoptic mange. see *Sarcoptes scabiei*
Satin moth. see *Stilpnotia salicis*
Sawfly, wheat stem. see *Cephus cinctus*
Saw-toothed grain beetle. see *Oryzaephilus surinamensis*
Say stink bug. see *Chlorochroa sayi*
Scale,
  apple oyster shell. see *Lepidosaphes ulmi*
  black. see *Saissetia oleae*
  Boisduval's. see *Diaspis boisduvali*
  California red. see *Aonidiella aurantii*
  camellia. see *Lepidosaphes camelliae*
  citricola. see *Coccus pseudo-magnoliarum*
  cottony cushion. see *Icerya purchasi*
  cyanophyllum. see *Aspidiotus cyanophylli*
  dictyospermum. see *Chrysomphalus dictyospermi*
  fern. see *Pinnaspis aspidistrae*
  Florida red. see *Chrysomphalus aonidum*
Scale, *(Continued)*
  Glover's. see *Lepidosaphes gloverii*
  greedy. see *Aspidiotus camelliae*
  hemispherical. see *Saissetia hemisphaerica*
  latania. see *Aspidiotus lataniae*
  olive. see *Parlatoria oleae*
  palm. see *Chrysomphalus dictyospermi*
  purple. see *Lepidosaphes beckii*
  San José. see *Aspidiotus perniciosus*
  scurfy. see *Chionaspis furfura*
  soft. see *Coccus hesperidum*
  tortoise. see *Coccus hesperidum*
  yellow. see *Aonidiella citrina*
Scale insects. see *Aonidiella, Aspidiotus, Chionaspis, Coccus, Lepidosaphes, Chrysomphalus, Diaspis, Icerya, Parlatoria, Pinnaspis, Saissetia*
Scapteriscus, 11
Scapteriscus ucletus (mole cricket), 30
Scarabeids, 2
Schistocerca (locust), 7; 13; 162
Schistosoma mansoni (platyhelminth; parasitic blood-fluke of man), 140
Schizanthus (plant genus), 166
Schoene's mite. see *Tetranychus schoenei*
Schoenocaulon officinale (plant), 149; 159
Sciara, 141
Scirtothrips citri (citrus thrips), 5
Scirtothrips signipennis (banana thrip; Australian), 13
Scleroracus vaccinii (blunt-nosed cranberry leafhopper), 17
Scobius, 140
Scolothrips sexmaculatus, 17
Screw-worm(s). see *Callitroga hominivorax, Cochliomyia americana, Cochliomyia macellaria*
Screw-worm, secondary. see *Cochliomyia macellaria*
Scurfy scale. see *Chionaspis furfura*
Scymnus binaevatus (a lady beetle), 17; 183
Scymnus creparus (a lady beetle), 59
Scymnus haemorhous (a lady beetle), 59
Scymnus syriacus (a lady beetle), 59
Secale cereale (plant), 170
Secondary screw-worm. see *Cochliomyia (=Callitroga) macellaria*
Seed-corn maggot. see *Hylemya cilicrura*
Selenia tetralunaria, 76; 78
Septanychus, 134; 138
Septanychus desertorum (desert mite), 134
Septanychus schoenei, 15
Septanychus texazona, 36; 59; 93; 126
Serpentine leaf miner. see *Liriomyza pusilla*
Sesamum indicum (plant), 149; 159; 171
Seventeen year locust. see *Cicada (=Magicicada) septendecim*
Shaft louse. see *Menopon gallinae*
Sheep,
  ked. see *Melophagus ovinus*
  tick. see *Melophagus ovinus*
Short-nosed cattle louse. see *Haematopinus eurysternus* and *Linognathus vituli*
Silkworm, domestic. see *Bombyx mori*
Silverfish. see *Lepisma saccharina*
Simarubaceae (plant family), 149
Simulium (black flies), 2; 16; 30; 56
Simulium damnosum (one of the black flies), 17; 138
Simulium venustum (one of the black flies), 120
Simulium vittatum (one of the black flies), 120
Siphona (=Haematobia), 142
Siphona exigua, 183
Siphona irritans (=Haematobia irritans) (horn fly), 16; 22; 30; 50; 120
Sitodrepa panicea (=Stegobium paniceum) (drug store beetle), 184
Sitona cylindricollis (sweet clover weevil), 11
Sitona hispidula (clover root curculio), 13; 138
Sitophilus, 1; 23; 30; 99; 114; 124; 171
Sitophilus granarius (granary weevil), 1; 2; 9; 13; 16; 17; 23; 28; 29; 37; 51; 52; 69; 76; 86; 87; 88; 89; 90; 99; 101; 104; 107; 114; 117; 121; 122; 123; 124; 125; 132; 134; 135; 138; 146; 147; 150; 151; 152; 160; 169; 170; 171; 183; 184; 185; 186
Sitophilus oryza (=Sitophilus oryzae), 4
Sitophilus oryzae (rice weevil), 1; 13; 23; 28; 29; 37; 45; 51; 52; 69; 82; 86; 87; 88; 89; 90; 101; 104; 114; 117; 121; 122; 146; 150; 169; 184; 185; 186
Sitotraga, 99
Sitotraga cerealella (angoumois grain moth), 28; 29; 104; 114; 121; 122; 170
Small body louse. see *Menopon gallinae*

Note: The numbers following the entries indicate the Section in which the entry occurs.

Smerinthus ocellatus, 154; 157
Smilax (plant genus), 141
Smynthurus viridis, 17
Soft scale. see *Coccus hesperidum*
Solanaceae (plant family), 149
Solenopsis, 112
Solenopsis geminata (fire ant), 181
Solenopis saevissima (imported fire ant), 30
Solenopotes capillatus (one of the cattle blood sucking lice), 30; 114
Sorbaria sorbifolia (plant), 117; 145
Sorghum halepense (plant), 170
Sorghum vulgare (plant), 170
Southern,
  armyworm. see *Prodenia eridania*
  green stink bug. see *Nezara viridula*
  house mosquito. see *Culex quinquefasciatus*
Sow bug(s). see *Armadillidium nosatum*
Sphaerophoria flavicauda, 59
Sphenarium purpurascens, 2; 13; 30; 56; 81; 108; 138; 183
Spider, black widow. see *Latrodectus mactans*
Spider mite,
  spruce. see *Paratetranychus ununguis*
  two-spotted. see *Tetranychus bimaculatus*
Spider mite(s), red. see *Paratetranychus citri, Tetranychus sexmaculatus, T. lewisi*
Spilonota ocellana (eye-spotted bud moth), 17; 75; 138
Spinose ear-tick, (Texas, Mexico). see *Ornithodoros megnini*
Spittlebug, meadow. see *Philaenus leucophthalmus*
Spittlebugs. see *Aphrophora* spp., *Philaenus leucophthalmus*
Spotted cucumber beetle. see *Diabrotica undecimpunctata*
Spring cankerworm. see *Paleacrita vernata*
Spruce,
  budworm. see *Choristoneura fumiferana*
  spider mite. see *Paratetranychus ununguis*
Squash,
  bug. see *Anasa tristis*
  borer. see *Melittia satyriniformis*
Stable fly. see *Stomoxys calcitrans*
Stegobium (=Sitodrepa) paniceum (Drug store beetle), 1; 28; 37; 86; 87; 88; 89; 101; 104; 114; 121; 122
Stemonaceae (plant family), 149
Stemona tuberosa (plant), 149
Stethorus pictipes, 17
Stethorus punctillum, 17
Stethorus punctum, 17; 183
Stilpnotia salicis (satin moth), 154; 157
Stink bug,
  Arizona brown. see *Euschistus impictiventris*
  Say. see *Chlorochroa sayi*
  southern green. see *Nezara viridula*
Stomoxys, 2; 73
Stomoxys calcitrans (stable fly), 22; 50; 96; 103; 154
Strawberry,
  aphid. see *Capitophorus fragaefolii*
  leaf roller. see *Ancylis comptana*
  root aphid. see *Aphis forbesi*
  weevil. see *Anthonomus signatus*
Strelitzia sp. (plant), 122
Sugarbeet root aphid. see *Pemphigus betae*
Sugarcane,
  frog hopper. see *Tomaspis saccharina*
  moth borer. see *Diatraea saccharalis*
Sweet clover weevil. see *Sitona cylindricollis*
Sweet-potato weevil. see *Cylas formicarius*
Syringa sp. (plant), 117; 145
Syrpha, 20; 132
Syrphids, 18; 20
Syrphus, 17

T

Tabanus (horse flies), 22. also see *Chrysops*
Tachypterellus quadrigibbus (apple curculio), 50
Taeniothrips, 13
Taeniothrips inconsequens (pear thrips), 30; 130
Taeniothrips simplex (gladiolus thrips), 30; 130
Tarnished plant bug. see *Lygus oblineatus, L. pratensis*
Tarsonemus latus, 26; 168
Tarsonemus pallidus (cyclamen mite), 59; 122; 130; 132; 138; 168; 178
Tenebrio (mealworms), 114; 134; 157
Tenebrioides mauritanicus (Cadelle; cadelle beetle), 28; 29; 52; 87; 88; 104; 114; 121; 122; 146; 185
Tenebrio molitor (yellow mealworm), 3; 17; 52; 117; 129; 130; 132; 134; 135; 138; 154; 157; 158; 179; 184
Tenebrio obscurus (dark mealworm), 122
Tenuipalpus, 138
Tephrosia (plant genus), 157
Tephrosia piscatoria (plant), 157
Tephrosia purpurea (plant), 157
Tephrosia toxicaria (plant), 157
Tephrosia virginiana (plant), 149; 157
Tephrosia vogeli (plant), 157
Termite; common dry-wood. see *Kalotermes minor*
Termites, 112; 140; 174. also see *Cryptotermes, Kalotermes, Reticulotermes*
Tetracnemus pretiosus, 17; 183
Tetranychidae, 15; 173
Tetranychus, 13; 132; 168
Tetranychus atlanticus, 59; 132
Tetranychus bimaculatus (two-spotted spider mite), 10; 14; 15; 20; 24; 34; 35; 36; 53; 54; 55; 58; 59; 61; 63; 64; 75; 77; 83; 85; 93; 96; 109; 111; 117; 125; 126; 129; 130; 132; 134; 137; 138; 143; 172; 178; 179; 183; 188. also see Tetranychus telarius
Tetranychus desertorum (desert mite), 60; 65; 66; 69
Tetranychus lewisi (one of the red spider mites), 15
Tetranychus mcdanieli, 17
Tetranychus pacificus (Pacific mite), 15; 17; 35; 36; 54; 55; 77; 96; 126; 138
Tetranychus schoenei (Schoene's mite), 17
Tetranychus sexmaculatus (one of the red spider mites), 15
Tetranychus telarius, 15; 17; 20; 31; 34; 35; 53; 54; 55; 59; 80; 104; 113; 129; 130; 132; 135; 140; 141; 157; 166; 172; 183. also see Tetranychus bimaculatus
Tetranychus urticae, 83; 85
Texas-fever tick. see *Boöphilus annulatus*
Thaumetopoea processionaria (processional caterpillar), 143
Theobaldia longeareolata, 17
Thermobia (firebrats), 163
Thermobia domestica (firebrat), 11; 52; 122; 130; 154; 157; 163
Thrips (genus), 157
Thrips,
  banded greenhouse. see *Hercinothrips femoralis*
  bean. see *Hercothrips fumipennis*
  citrus. see *Scirtothrips citri*
  flower. see *Frankliniella cephalica, F. tritici, Thrips tritici*
  gladiolus. see *Taeniothrips simplex*
  greenhouse. see *Heliothrips haemorrhoidalis*
  iris. see *Bregmatothrips iridis*
  onion. see *Thrips tabaci*
  pear. see *Taeniothrips inconsequens*
  tobacco. see *Frankliniella fusca*
Thrips. see *Bregmatothrips, Frankliniella, Haplothrips, Heliothrips, Hercinothrips, Hercothrips, Leptothrips, Scirtothrips, Taeniothrips, Thrips*
Thrips nigropilosus, 17; 130
Thrips tabaci (onion thrips), 2; 13; 17; 26; 30; 59; 77; 96; 129; 130; 132; 141; 156; 157; 183
Thrips tritici (flower thrip), 141
Thyridopteryx ephemeraeformis (bagworm), 13; 112; 138; 183
Tick,
  American dog. see *Dermacentor variabilis*
  castor bean. see *Ixodes ricinus*
  cattle. see *Boöphilus annulatus*
  fowl. see *Argas persicus*
  Gulf Coast. see *Amblyomma maculatum*
  lone star. see *Amblyomma americanum*
  Rock Mountain wood. see *Dermacentor andersoni*
Ticks. see *Amblyomma, Argas, Argasidae, Boöphilus, Dermacentor, Ixodes, Ornithodoros, Rhipicephalus*
Tick(s), fever. see *Boöphilus* spp.
Tier, celery leaf. see *Phlyctaenia rubigalis*
Tinea (clothes moth), 31
Tinea granella, 114
Tinea pellionella (case-making clothes moth), 129
Tineola bisselliella (webbing clothes moth), 13; 29; 50; 89; 101; 104; 122; 127; 129; 158; 169; 184; 186
Tipula (crane flies), 114
Tobacco,
  budworm. see *Heliothis virescens*
  flea beetle. see *Epitrix hirtipennis*
  hornworm. see *Protoparce sexta*
  moth. see *Ephestia elutella*
  thrips. see *Frankliniella fusca*
Tomaspis flavilatera, 13
Tomaspis saccharina (sugarcane frog hopper), 13
Tomato,
  fruitworm. see *Heliothis armigera*
  hornworm. see *Protoparce quinquemaculata*
  pinworm. see *Keiferia lycopersicella*
Torpedo (genus of fishes), 134
Tortoise scale (tortoise scale insects). see *Coccus* spp., *Saissetia* spp.
Tortricids, 16
Tortrix, orange. see *Argyrotaenia citrana*
Tortrix postvittana, 17
Tortrix pronubana, 13
Tournefortia hirsutissima (plant), 149
Towbug. see *Lasioderma serricorne*
Toxoptera aurantii (black citrus aphid), 20
Toxoptera graminum (greenbug), 46; 59; 138
Tremex columba (pigeon tremex), 28
Trialeurodes abutilonea, 132
Trialeurodes packardi, 130
Trialeurodes vaporariorum (greenhouse whitefly), 17; 23; 26; 100; 129; 130; 132; 138; 149; 157
Triatoma (kissing bug), 17
Tribolium, 23; 30; 76; 99; 104; 114; 130; 173
Tribolium castaneum (red flour beetle), 13; 17; 28; 29; 37; 76; 88; 89; 101; 104; 114; 121; 122; 124; 130; 135; 154; 157; 169; 173; 184; 186
Tribolium confusum (confused flour beetle), 1; 4; 9; 13; 17; 19; 28; 29; 37; 49; 51; 52; 57; 61; 74; 86; 87; 88; 89; 90; 94; 96; 97; 99; 101; 104; 114; 117; 119; 121; 122; 123; 124; 129; 130; 134; 135; 138; 139; 150; 151; 169; 170; 171; 177; 184; 185; 186
Tribolium confusum HCN-R biotype, 101
Trichobaris mucorea (tobacco stalk borer), 30
Trichogramma minutum, 17; 112
Trichoplusia, 17
Trichoplusia ni (cabbage leafhopper), 13; 16; 112; 114; 120; 156; 158; 159; 183
Trifolium pratensis (plant), 170
Tripterygium (plant genus), 188
Tripterygium wilfordii (plant), 149; 188
Triticum aestivum (plant), 170
Trogoderma, 17; 114
Trogoderma sternalis, 13
Trogoderma versicolor, 184
Trombicula, 14
Trombicula alfreddugesi, 91. also see *Eutrombicula alfreddugesi*
Trombicula irritans, 14; 168. also see *Eutrombicula alfreddugesi*
Trombicula masoni, 91
Trombicula splendens, 48; 73; 91
Trombiculid mites, 14; 48; 76
Trombiculids, 2; 13; 38
Tropical rat mite. see *Liponyssus bacoti*
Tsetse flies. see *Glossina morsitans, G. palpalis*
Tuber fleabeetle. see Epitrix tuberis
Tuberworm, potato. see *Gnorimoschema operculella*
Turnip aphid. see *Rhopalosiphum pseudobrassicae*
Tussock moths. see *Lymantria* spp.
Two-spotted,
  lady beetle. see *Adalia bipunctata*
  spider mite. see *Tetranychus bimaculatus*
Two-striped grasshopper. see *Melanoplus bivittatus*
Tychius griseus (a red clover weevil), 13; 138
Typhlociba comes (apple leafhopper), 157
Typhlodromus, 17; 31; 59

U

Ulmus americana (plant), 117; 145
Umbelliferae (plant family), 149

V

Vanessa (=Cynthia), 7; 94; 134; 139; 163
Vanessa antiopa, 132; 134

Note: The numbers following the entries indicate the Section in which the entry occurs.

Vanessa cardui (Painted lady), 77; 78; 112; 157
Vanessa io, 143; 154; 157
Vanessa polychloros, 154; 157
Vanessa urticae, 154; 157; 162
Variegated cutworm. see *Peridroma margaritosa, Lycophotia margaritosa*
Vasates cornutus (silver mite, peach), 138
Vasates lycopersicae, 17
Vedalia (lady beetle). see *Rodolia cardinalis*
Vegetable weevil. see *Listroderes costirostris obliquus*
Velvetbean caterpillar. see *Anticarsia gemmatilis*
Veratrum album (plant), 149; 159
Veratrum viride (plant), 149; 159
Veronica (plant genus), 170
Vespula (hornets), 13
Viburnum dilatatum (plant), 117; 145
Viburnum lantana (plant), 117; 145
Vicia faba (plant), 132; 137; 164; 170; 172; 184
Vigna sinensis (plant), 170
Vinegar fly. see *Drosophila melanogaster*
Vitaceae (plant family), 149

W

Walnut,
  aphid. see *Chromaphis juglandicola*
  caterpillar. see *Datana integerrima*
  husk fly. see *Rhagoletis completa*
Wasmannia auropunctata (little fire ant), 138; 183
Wasps, paper nest. see *Polistes*
Wattle bagworm. see *Acanthopsyche junodi*
Wax moth. see *Galleria mellonella*
Webbing clothes moth. see *Tineola bisselliella*
Webworm,
  beet. see *Loxostege sticticalis*
  Fall. see *Hyphantria cunea*
  garden. see *Loxostege similalis*
Weevil,
  alfalfa. see *Hypera postica*
  bean. see *Acanthoscelides obtectus*
  boll. see *Anthonomus grandis*
  cowpea. see *Callosobruchus maculatus*
  granary. see *Sitophilus granarius;* also see *Calandra granaria (=Sitophilus granarius)*
  pea. see *Bruchus pisorum*
  pepper. see *Anthonomus eugenii*
  rice. see *Sitophilus oryzae*
  strawberry. see *Anthonomus signatus*
  sweet clover. see *Sitona cylindricollis*
  sweet potato. see *Cylas formicarius*
  vegetable. see *Listroderes costirostris obliquus*
Western corn rootworm. see *Diabrotica virgifera*
Wheat,
  stem sawfly. see *Cephus cinctus*
  wireworm. see *Agriotes mancus*
Whitefly; whiteflies. see *Aleurocanthus woglumi, Dialeurodes citri, Trialeurodes vaporariorum*
Whitefly, citrus. see *Dialeurodes citri*
Winter moth. see Operophthera brumata
White-fringed beetle. see *Graphognathus leucoloma, Pantomorus leucoloma*
Wireworm,
  Pacific Coast. see *Limonius canus*
  sand (cotton). see *Horistonotus uhleri*
  wheat. see *Agriotes mancus*
Wood tick. see *Dermacentor variabilis, D. andersoni*
Worm,
  melon. see *Diaphania hyalinata*
  pickle. see *Diaphania nitidalis*

XYZ

Xenopsylla cheopis (oriental rat flea), 2; 73; 91; 96
Xylocopa violacea (a carpenter bee), 134
Yellow,
  fever mosquito. see *Aëdes aegypti*
  mealworm. see *Tenebrio molitor*
  necked caterpillar. see *Datana ministra*
  scale. see *Aonidiella citrina*
Zabrotes pectoralis, 1; 28; 37; 86; 87; 88; 89; 101; 104; 121; 122
Zabrotes subfasciatus, 28; 122
Zanthoxyllum clavaherculis (plant), 149
Zea mays (plant), 132; 137; 138; 170; 183
Zeuzera pyrina (leopard moth), 28; 130
Zygadenus venenosus (plant), 159

Note: The numbers following the entries indicate the Section in which the entry occurs.

INDEX OF CHEMICAL COMPOUNDS

Note: The numbers following the entries indicate the Section in which the entry occurs.

2, 4-D, 141
88R (Eighty-eight R), 24
612 Insect Repellent, 91
666 (Six-six-six), 114
1080 (Ten eighty), 164
3960 x 14, B. F. Goodrich Chemical Co., 167
A 12 oil, 154

A

Acaricides, 126
Acenaphthene, 141
Acetate Rayon, 170
Acetic ether, 84
Acetoacetic acid, cyclohexyl ester, 155
Acetone, 104
Acetonitrile, 1
Acetylacetone, 104
Acetyl chloride, 104
Acetylcholine, 134
N-Acetyl-2,3,9,10-dibenzophenothiazine, 142
N-Acetyl-2,3,9,10-dibenzophenothiazone, 142
Acetyl dihydrorotenolone, 157
Acetyl dihydrorotenone, 157
N-Acetyl-3,9-dimethylphenothiazine, 142
Acetylene tetrachloride, 176
Acetyl indan(e)dione, 110; 148
Acetyl-β-methylcholine, 134
N-Acetylphenothiazine, 142
Acetyl rotenolone, 157
Acetyl rotenone, 157
Acid copper arsenite, 7
Acid lead arsenate, 112
Acridine, 131
Acridines, 141
Acrolein, 103
Acrylonitrile, 1
Actomyosin, 158
Acylated 1,3-indandiones, 148
2-Acyl substituted-1,3-indandiones, 148
Adenosine diphosphate, 158
Adenosine triphosphate, 134; 158
Alcohols, 154
Aldehydes, 154
Aldrin, 2, 174
Aliphatic thiocyanates, 135
Alkron, 138
Alkyl acid phosphate esters: Amyl, Butyl, Ethyl, Isopropyl, Loralkyl(s), Methyl, Octyl, Propyl, 134
Alkyl fluorophosphonates, 18
Alkyl formates, 90
Allethrin, 3
α-*dl*-Allethrin (trans), 3
Allethrin, ethyl analogue of, 3
Allethrin, methyl analogue of, 3
Allethrin, 3,4-methylenedioxybenzyl analog, 171
Alltox, 183
Allyl bromide, 4
Allyl chloride, 82
Allyl formate, 82
dl-2-Allyl-4-hydroxy-3-methyl-2-cyclopenten-1-one ester of cis-trans-*dl*-chrysanthemum monocarboxylic acid, 3
Allyl iodide, 82
Allyl isothiocyanate, 23
2-Allyl-3-methyl-2, 4-cyclopentadienone, 3
dl-2-Allyl-3-methylcyclopent-2-3n-4-ol-1-onyl *dl*-cis-trans-chrysanthemate, 3
Allyl pentachlorophenyl ether, 140
Allylrethrolone, 3
dl-Allylrethronyl *dl*-cis-trans-chrysanthemate, 3
Aluminum (= aluminium), 170
Aluminum arsenate, 7
Aluminum stearate, 141
American Cyanamid Company 3911, 60
Amidohalogenophosphates (compound group), 134
Amino-acids, 154
4-Aminoazobenzene, 126
4-Aminobenzene, 126
p-Aminophenol, 134
p-Aminophenyl glucuronide, 138
Aminophylline, 138
p-Aminopropiophenone, 135
Ammonia, 104
Ammonium fluoaluminate, 42
Ammonium p-chlorobenzene sulfonate, 17
Amorphous veratrine, 159
Amphetamine, 93
Amyl acetate, 165
Amyl alcohol (tertiary), 104
Amyl bromide, 104
N-Amylimide, 92
2-Amyl-6-methyl-pyridine, 104
Amyl pentachlorophenyl ether primary, 140
4-n-Amyl-piperidine, 104
Amyl propionate, 104
2-n-Amyl-pyridine, 104
4-n-Amyl-pyridine, 104
Anabasine, 5
Anabasine sulfate, 5
Anabasis aphylla, 5
Anacardic acid (chlorinated), 174
Anatabine, 130
Anhydroryanodine, 158
Anise (oil of), 149
Anisic chrysanthemic acid ester, 3
Anisolactone, 103
Anthracene, 141
Anthracene oil, 141
Antibiotics, 6
Antimetabolites, 6
Antinnonin, 76
Aphyllidine, 5
Aphylline, 5
Araclor 5460, 3
Aramite®, 24
Aromatic nitriles, 1
Arsenic, 7
"Arsenic", 8
Arsenic acid, 7
Arsenicals, 7
Arsenic (pentavalent), 25; 139
Arsenic pentoxide, 7
Arsenic sesquioxide, 8
Arsenic trichloride, 104
Arsenic trioxide, 8
Arsenic (trivalent), 25; 139
Arsenious acid, 7
Arsenious acid anhydride, 8
Arsenious oxide, 8
Arsenomethane As-1,2-disulfide, 9
Arsenomethane disulfide, 9
Arsine(s), 139
Arsonated Toxaphene®, 183
Aryl phosphonic acids: p-chlorobenzene, 3,4-di-
Aryl phosphonic acids: *(Continued)*
3,4-dichlorobenzene, 134
Asagraea officinalis, 159
Asarinin, 160; 171
ASP-47, 178
Asphaltic oils, 141
Asphaltic petroleums, 141
Atropine, 3; 93; 134; 137; 138
Attaclay, 9
Aureomycin, 6
Auricula (plant genus), 132
Azobenzene, 10
Azobenzide, 10
Azobenzol, 10
Azoxybenzene, 10

B

Bacitracin, 6
BAL, 7
Barbasco, 157
Barden clay, 170
Barium arsenate, 7
Barium fluoride, 94
Barium fluosilicate, 11
Barium oxide, 7
Barium silicofluoride, 11
Basic copper arsenate, 7
Basil (oil of), 149
Bayer L 13/59, 74
Bayer 22/190, 69
Bayer 17147, 16
Bees and insecticides, 12
Beneficial insects and insecticides, 12
Benzahex, 114
Benzaldehyde, 101
Benzaldehyde phenylhydrazone, 126
Benzene, 104; 141
Benzene azobenzene, 10
Benzeneazo-o-cresol, 126
Benzene-azo-β-naphthol, 154
Benzene heptachloride, 13
Benzene hexachloride, 13
γ-Benzene hexachloride, 114
Benzil, 38
Benzimidazole, 6
Benzinoform, 29
Benzinol, 186
Benzoic acid, benzyl ester, 14
Benzoic acid, 2-chlorophenyl ester, 14
Benzoic acid, 3,5-dimethylphenyl ester, 14
Benzoic acid, a-methylbenzyl ester, 14
Benzoic acid, phenyl ester, 14
Benzoic acid, phenylethyl ester, 14
Benzoin, 126
Benzonitrile, 1
Benzophenone, 126
Benzoylcholine, 134
Benzoyl indan(e)dione, 110, 148
Benzyl alcohol, 157
Benzylamine benzyl dithiocarbamate, 126
Benzyl benzene carboxylate, 14
Benzyl benzoate, 14
Benzyl bromide, 101
Benzyl chrysanthemic acid ester, 3
Benzyl cyanide, 1
Benzyl pyridine, 131
Benzyl thiocyanate, 135

Benzyl trichlorophenol, 140
BFPO, 18; 172
BHC, 13; 174
γ-BHC, 114
BHC γ-isomer, ~~174~~ 114
Bicyclodihydrofuran symmetrically substituted by 2 methylenedioxyphenyl groups, 171
Bicyclo (2,2,1)-heptene-2,3-dicarboxylic acid, dimethyl ester, cis-dimethyl carbate, 155
Bis-(bis-dimethylamido) pyrophosphate, 172
Bis-(bis-dimethylamino) phosphonous anhydride, 132
Bis-(3-brom-4-methoxyphenyl) trichloroethane, 17
Bis-(5-bromnaphthyl) trichloroethane, 17
Bis-(p-bromophenoxy)-methane, 15
Bis-(p-bromophenyl) methane, 17
Bis-(2-chlor-5-methylphenyl) trichloroethane, 17
Bis-(5?-chlornaphthyl) trichloroethane, 17
N,N-Bis-(2-chloroethyl) methylamine hydrochloride, 6
0,0-Bis-(2 chloroethyl) S-tert.-butylmercaptomethyl dithiophosphate, 134
1,1-Bis-(5-chloro-2-hydroxyphenyl) ethane, 17
Bis-(5-chloro-2-hydroxyphenyl) methane, 17
Bis-(p-chlorophenoxy)-methane, 15
Bis-(p-chlorophenyl) acetamide, 17
Bis-(p-chlorophenyl) acetic acid, 17
2,2-Bis-(p-chlorophenyl)-1-chloroethylene, 16
2,2-Bis-(p-chlorophenyl)-1,1-dichloroethane, 16
2,2-Bis-(p-chlorophenyl)-1,1-dichloroethylene, 17; 171
1,1-Bis-(p-chlorophenyl)-ethanol, 15; 54; 171
Bis-(p-chlorophenyl) ethinyl carbinol, 12; 54
Bis-(p-chlorophenyl)-methane, 15; 17; 54
Bis (p-chlorophenyl) methanol, 17
1,1-Bis-(p-chlorophenyl) methanol, 54
Bis-(p-chlorophenyl) methyl carbinol, 54
Bis-(p-chlorophenyl) methyl methyl ether, 17
Bis-(p-chlorophenyl) sulfone, 17
2,2-Bis-(o-chlorophenyl)-1,1,1-trichloroethane, 17
α,α-Bis-(p-chlorophenyl)-β,β,β,-trichloroethane, 17
2,2-Bis-(p-chlorophenyl)-1,1,1-trichloroethane, 17
3,3-Bis-(p-chlorophenyl)-2,1,1-trichloropropene, 17
2,2-Bis-(p-chlorophenyl)-1,1,1-trifluoroethane, 17
Bis-(4-chlor-3-sulfaphenyl)-trichloroethane disodium, 17
Bis-(diamylamino)-fluorophosphine oxide, 134
Bis-(3,5-dichloro-2-hydroxyphenyl) methane, 17
Bis-(dicyclohexylamino)-fluorophosphine oxide, 134
Bis- (2,5-dimethoxyphenyl) trichloroethane, 17
Bis-(3,4-dimethoxyphenyl) trichloroethane, 17
N,N-Bis-(dimethylamido)-O-o-aminophenyl phosphate, 134
N,N-Bis-(dimethylamido)-O-p-aminophenyl phosphate, 134
Bis-(dimethylamido) diethyl pyrophosphate (asym.), 172
Bis-(dimethylamido) diethyl pyrophosphate (sym.), 172
Bis-(dimethylamido)-p-nitrophenyl phosphate, 134
N,N-Bis-(dimethylamido)-O-p-nitrophenyl phosphate, 134
Bis-(dimethylamido) phosphorofluoridate, 132
Bis-(dimethylamino)-fluorophosphate, 18
Bis-(dimethylamino)-fluorophosphine oxide, 18, 172
Bis-(dimethylamino)-p-nitrophenyl phosphate, 18
S-1:2-Bis-(ethoxycarbonyl) ethyl-O,O-dimethyl, thiophosphate, 117
2,2-Bis-(p-ethylphenyl)-1,1-dichloroethane, 50
2,2-Bis-(p-fluorophenyl)-1,1-dichloroethane, 17
2,2-Bis-(p-fluorophenyl)-1,1-dichloroethylene, 17; 19
2,2-Bis-(p-fluorophenyl)-1,1,1-trichloroethane, 19
3,3-Bis-(p-fluorophenyl)-2,1,1-trichloropropene, 17
2,2-Bis-(p-fluorophenyl)-1,1,1-trifluoroethane, 17
Bis-(hydroxyphenyl)-trichloroethane, 17
2,2-Bis-(p-methoxyphenyl)-1,1-dichloroethylene, 120
2,2-Bis-(p-methoxyphenyl)-1,1,1-trichloroethane, 120
Bis-(2-methyl-4-chlorphenyl) trichloroethane, 17
Bis-(p-methylphenoxy)-methane, 15; 54
Bis-(2,4-methylphenyl) trichloroethane, 17
Bis-(monoisopropylamino) fluorophosphate, 20
Bis-(monoisopropylamino)-fluorophosphine oxide, 20; 172
Bis-(naphthyl)-trichloroethane, 17
Bis-(3-nitro-4-chlorphenyl) trichloroethane, 17
Bis-(substituted-phenoxy)-methanes, 15
Bis-(2,4,6-trichloro-3-hydroxyphenyl) methane, 17
Bituminous coal tar, 141
Blacosolv, 186
Bladafume, 178
Bladan, 100; 179
Bladex, 179
Body lice; tests of insecticides against, 128
Bonoform, 176
Borax, 21
Borneol, chrysanthemic acid ester of, 3
Brass, 170
Brilliant green, 39
Brimstone, 168
British anti-Lewisite, 7
Brombenzene, 104
"Bromine-DDT", 17
Bromoallylene, 4
Bromobenzene, 166
1-Bromo-3-chloro-butane, 82; 104
1-Bromo-2-chloroethane, 104
1-Bromo-3-chloro-propane, 82; 104
2-Bromo-1-chloro-propane, 82; 104
Bromocyclopentane, 82; 104
2-Bromoethyl acetate, 82
2-Bromoethyl ethyl ether, 82
Bromoform, 104
Bromofume, 87
5-Bromo-2-isovaleryl indanedione, 110
Bromomethane, 122
Bromonaphthalene, 129
9-Bromophenanthrene, 129
4-(p-Bromophenylazo)-m-cresol, 10
4-(p-Bromophenylazo)-o-cresol, 10
1-(p-Bromophenylazo)-2-naphthylamine, 10
p-Bromophenylazophenol, 10
4-(p-Bromophenylazo)-resorcinol, 10
4-(p-Bromophenylazo)-5,6,7,8-tetrahydro-1-naphthol, 10
Bromopicrin, 104
3-Bromopropene, 4
3-Bromopropylene, 4
γ-Bromopropyl phenyl ether, 135
Bromostyrol, 104
α-Bromo-toluene, 82; 104
Bulan®, 174
Buna H rubber, 170
Buna rubber, 170
Butanol, 104
d-2-cis-(But-2'enyl)-3-methyl-cyclopent-2-en-4-ol-1-one, 154
d-cis-But-2-enylrethrolone, 154
But-2'-enylrethronyl *d*-trans-chrysanthemate, 3
Butopyronoxyl (USP), 103
α-Butoxy-N-cyclohexylamide, 91
α-(2-[2-n-Butoxyethoxy]-ethoxy)-4,5-methylenedioxy-2-propyltoluene, 146
α-(2-[2-n-Butoxyethoxy]-ethoxy)-4,5-methylenedioxy-2-propyltoluene-α-C^{14}, 146
2-(2-[Butoxy] ethoxy) ethyl ether of thiocyanic acid, 23
2- Butoxyethyl-3,4-methylenedioxyphenyl-acetal-aldehyde, 171
2-Butoxyethyl thiocyanoacetate, 106; 135
Butoxy polypropylene glycols 400 and 800, 22
β-Butoxy-β'-thiocyanodiethyl ether, 23
2-Butoxy-2'-thiocyanodiethyl ether, 23
N-Butylacetanilide, 91
Butyl alcohol (tertiary), 104
Butylamine, 82; 104
n-Butylamine, 104
Butyl bromide, 97; 104
Butyl bromide (tertiary), 82
n-Butyl bromide, 4
Butyl butyrate, 104
N-Butyl-butyrol thialdine, 126
Butylcarbamic acid, 3,4-methylenedioxyphenyl ester, 171
Butyl carbitol rhodanate, 23
Butyl carbitol thiocyanate, 23; 135
Butyl carbityl-6-(propylpiperonyl) ether, 146
Butyl cellosolve, 133
n-Butyl chloride, 104
Butyl chloride (tertiary), 104
4-tert.-Butylcyclohexyl thiocyanoacetate, 106; 135
Butyl - DDT, 174
2-sec.-Butyl-4,6-dinitrophenol, 75
n-Butyl disulfide, 126
n-Butyl ester of 3,4-dihydro-2,2-dimethyl-hexo-2H-pyrone-6-carboxylic acid, 103
5-Butyl-5-ethyl-2-3,4,-methylenedioxyphenyl-m-dioxane, 171
2-Butyl-2-ethyl-1,3-propanediol, 91
N-Butylimide, 92
2-tert.-Butyl-1,3-indan(e)dione, 148
Butyl iodide (secondary), 104
n-Butyl iodide, 104
n-Butyl mercaptan, 104; 126
S-tert.-Butylmercaptoethyl O,O-bis-(2-chloroethyl) dithiophosphate, 134
n-Butyl mesityl oxide oxalate, 103
Butyl-3,4-methylenedioxyphenyl-acetal-acetaldehyde, 171
2- Butyl-6-methyl-pyridine, 104
n-Butyl nitrite, 104
n-Butyl pentachlorophenyl ether, 140
Butylphenoxyisopropyl chloroethyl sulfite, 24
2-(p-tert.-Butylphenoxy)-isopropyl-2-chloroethyl sulfite, 24
m-tert.-Butylphenyldiethyl phosphate, 134
m-tert.-Butylphenyl-N-methylcarbamate, 134
n-Butyl phthalate, 48
2-n-Butyl-pyridine, 104
4-n-Butyl-pyridine, 104
α-n-Butyl pyrrolidine, 130
N-Butylpyrrolidine, 130
α-n-Butyl pyrroline, 130
Butyl rubber, 170
n-Butyl sulfide, 126
Butyl tetrachlorophenoxyethyl acetate, 140
N-Butyl-1,2,3,6-tetrahydrophthalamide, 91
n-Butyl thiocyanate, 104; 135
Butyl thiocyanate (tertiary), 126
Butylvalone (tertiary), 148
N-Butyronitrile, 1
Butyrylcholine, 134
Butyryl indanedione, 110

C

Caffeine, 93
Calcium arsenate, 25
Calcium cyanide, 26
Calcium 2,4-dinitro-6-cyclohexylphenate, 77
Calcium meta-arsenate, 7
Calcium oxide, 7
Calcium thiosulfate, 113
Calomel, 118
Camphene, 166
2-Caproxyethyl thiocyanoacetate, 106; 135
Caproyl indanedione, 110
N-Caprylcolaminoformyl methylpyridinium chloride, 6
Capryl thiocyanoacetate, 106; 135
Carbachol, 134
Carbamates, 27
Carbamic acid esters, 27
S-Carbamyl O,O-dimethyl dithiophosphate, 134
S-Carbamylmethyl diethyl dithiophosphate, 134
Carbazole, 141
N-Carbethoxymethyldiethyl phosphoroamidothionate, 6
Carbitol, 157
2-Carbo-n-butoxy-6,6-dimethyl-5,6-dihydro-1,4-pyrone, 103
Carbolic acid soaps, 141
Carbolic oils, 141
Carbolineums, 141
Carbon bisulfide, 28
Carbon bisulphide, 28
Carbon dichloride, 177
Carbon dioxide, 104
Carbon disulfide, 28
Carbon disulphide, 28
Carbon hexachloride, 98
Carbonic acid, 165
Carbon tetrabromide, 104
Carbon tetrachloride, 29
Carboxide, 99
N-2-Carboxyethyl diethyl phosphoramidothionate, 6
Cardol (chlorinated, crude), 174
Carvomenthyl thiocyanoacetate, 106; 135
Castor oil, 154; 157
Caustic barley, 159
CD-68; 30

Note: The numbers following the entries indicate the Section in which the entry occurs.

Cecolene, 186
Cellon, 176
CES, 24
Cevadilla, 159
Cevadine, 159
Chem Hex, 114
Chenopodiaceae, 5
2'-Chlorallylrethrolone, 3
3'-Chlorallylrethrolone, 3
Chlorbenside, 31
Chlorbenzene, 104
2-Chlorbutene-2, 104
Chlordan(e), 30; 174
Chlordane (cis), 96
Chlordane (trans), 96
Chlorex®, 51
Chlorinated camphene, 183
Chlorinated propane - propylene mixture, 45
3-Chloroacenaphthene, 129
Chloroacetonitrile, 1; 184
2-Chloroacetonitrile, 1
2-Chloroacrylonitrile, 1
Chloroarsenomethane As-1,2-disulfide, 9
4-Chloroazobenzene, 126
Chlorobenzene, 17
Chlorobenzilate, 85
p-Chlorobenzophenone, 17
Chlorobenzylate, 85
p-Chlorobenzyl-p-bromophenyl ether, 15
p-Chlorobenzyl-p-chlorophenyl ether, 15; 54
p-Chlorobenzyl-p-chlorophenyl sulfide, 31
p-Chlorobenzyl-*dl*-trans-chrysanthemate, 154
o-Chlorobenzyl cyanide, 1
p-Chlorobenzyl cyanide, 1
1-Chloro-2,2-bis(p-chlorophenyl) ethane, 17
Chloro-bis-(p-chlorophenyl) methane, 17
Chlorobromopropene, 32; 104
1-Chloro-3-bromopropene-1, 32
3-Chlorobutyronitrile, 1
4-Chlorobutyronitrile, 1
1-Chloro-2-(β-chloroethoxy) ethane, 51
α-Chloro-α-o-chlorophenyl acetamide, 17
α-Chloro-α-p-chlorophenyl acetamide, 17
Chlorocide, 31
Chlorocyclopentane, 82, 104
4-Chlorodiphenyl sulfone, 36, 126
1-Chloro-2,3-epoxypropane, 82
β-Chloroethyl- β' -(p-tert.-butylphenoxy)-α-methylethyl sulfite, 24
β-Chlorethyl-β' -(p-tert.-butylphenoxy)-β-methylethyl sulfite, 174
2- Chloroethyl ether, 82
2'-Chloroethyl-1-methyl-2-(p-tert.-butylphenoxy)-ethyl sulfite, 24
2-Chlorofluorene, 129
1-Chloro-4-iodobutane, 82, 104
γ-Chloroisobutylene, 121
2- Chloroisobutyronitrile, 1
Chloromethyl-p-chlorophenyl sulfone, 33
Chloromethyl-4-chlorophenyl sulfone, 33
4-Chloro-4'-methyldiphenyl sulfone, 126
Chloromethyl ether, 104
Chloromethyl oxirane, 82
3-Chloro-2-methyl-1-propene, 121
3-Chloro-2-methylpropene-1, 121
α-Chloronaphthalene, 129
β-Chloronaphthalene, 129
Chloroparacide, 31
Chloroparicide, 31
p-Chlorophenacyl-*dl*-trans-chrysanthemate, 154
p-Chlorophenethyl-*dl*-trans-chrysanthemate, 154
Chlorophenothane, 17
p-Chlorophenyl benzene sulfonate, 34
4-Chlorophenyl benzene sulfonate, 34
p-Chlorophenyl-p-chlorobenzene sulfonate, 35
4-Chlorophenyl-4-chlorobenzene sulfonate, 35
p-Chlorophenyl-p-chlorobenzoate, 15; 54
p-Chlorophenyl-p-chlorobenzyl sulfide, 31
p-Chlorophenyl-chloromethyl sulfone, 33
2-o-Chlorophenyl-2-p-chlorophenyl-1,1-dichloroethane, 17
2-o-Chlorophenyl-2-p-chlorophenyl-1,1,1,-trichloroethane, 17
p-Chlorophenyl *dl*-cis-chrysanthemate, 154
p-Chlorophenyl-*dl*-trans-chrysanthemate, 154
p-Chlorophenyl diethyl phosphate, 100; 126
3-(p-Chlorophenyl)-1,1-dimethyl urea, 12
1-o-Chlorophenylethyl-2-trichloro-p-chlorobenzene sulfonate, 17
p-Chlorophenyl phenyl dichloromethane, 17
p-Chlorophenyl phenyl sulfone, 36
2-(p-Chlorophenyl)-1,1,1,2-tetrachloroethane, 17
1-o-Chlorophenyl-2-trichloroethanol-1, 17
1-p-Chlorophenyl-2-trichloroethanol-1, 17
2-(p-Chlorophenyl)-1,1,1,-trichlorethanol, 15; 54
1-o-Chlorophenyl-2-trichlorethyl-p-chlorobenzene sulfonate, 17
Chloropicrin, 37
2-Chloropropionitrile, 1
3-Chloropropionitrile, 1
γ-Chloropropylene oxide, 82
α-Chloro-xylene, 82; 104
Chlorphenyl-hydroxy-trichloroethane, 17
Chlorpicrin, 37
Chlorthion®, 69
Chlorylen, 186
Chrysanthemic acid, 3
d-cis-Chrysanthemic acid, 154
d-trans-Chrysanthemic acid, 154
l-cis-Chrysanthemic acid, 154
dl-trans-Chrysanthemic acid, 154
Chrysanthemic acid esters: Acetopropyl alcohol, Allyl, Allylamine, Allyphenyl carbinol, o-Allyl vanillin, Amyl, Aniline, Benzal cyclopentanolone, Benzhydrol, Benzoin, Benzoyl alcohol, Benzyl alcohol, Benzylamine, Borneol, Capryl, Carvacrol, Cetyl, Cholestrin, Cinnamic alcohol, Citronellol, p-Cresol, Cyclopentanolones, Cyclopentenolones, Dextrose, Diacetone alcohol, 2,3-Dimethyl carbonester, Dimethyl hexenolone, α,α-Dimethyl phenethyl alcohol, Ethylamine, Ethylene chlorohydrin, Ethylene glycol, Ethyl lactate, Eugenol, Furfuryl alcohol, Geraniol, Guiacol, Heptyl, Hydroquinone, Hydroquinone diester, o-Hydroxybenzyl alcohol, Hydroxycamphor, Hydroxymethylene camphor, Isoeugenol, p-Isopropylbenzyl alcohol, Lauryl, Levulose, Linalool, Mannose, Menthol, o-Methoxyaniline, p-Methoxybenzyl alcohol, Methyl, 3-Methyl-2-allyl-2-allyl-2-carbonester, 3-Methyl carbonester, 3-Methyl-2-carbonester, Methylcyclohexanol, 3-Methyl-2-allyl-cyclopentenolone, 3-Methyl-5-allyl-cyclopentenolone, 2-Methyl Δ-3,4,5,6-heptadienol, Methyl mercaptan, 3-Methyl-2-propenyl, Methylsantonic acid, Methyl styryl carbinol, Monomethyl ether, Myristyl, p-Nitroaniline, Orcinol monomethyl ether, Phenol, 3-Phenylcarbonester, Phenylethyl alcohol, β-Phenylethylamine, Phenylpropyl alcohol, Piperonyl alcohol, Pyrocatechol, Phytol, 8-Quinolinol, Sabinol, Salicyl, 3-Styryl-cyclopentadiene dicarbonester, Styryl cyclopentenolone, α-Terpineol, Thiophenol, Thymol, 1-(p-Tolyl)-ethanol, Triphenyl carbinol, Vanillin
Chrysanthemum cinerariaefolium (powder or extracts of), 154
Chrysanthemum dicarboxylic acid monomethyl ether, 154
Chrysanthemumic acid, α-ethylpiperonyl ester, 134
Chrysanthemumic acid, α-isopropylpiperonyl ester, 134
Chrysanthemumic acid, a-propylpiperonyl ester, 134
Chymotrypsin, 132
Cinerin I analogues, various side-chains attached to the cyclopentenolone nucleus, side-chain saturation at ketoposition, etc., 154
Cinerolone, 154
Cinerolone esters of mono- and di-chrysanthemum carboxylic acids, 154
Cinerolone esters of various acids: Acetic, Benzoic, Camphor, Cinnamic, Citronellic, Crotonic, Dichloroacrylic, β-Fencholic, Geranium, Isobutyric, Malonic, o-Methoxybenzoic, Piñon, Undecylenic, 154
Cinerolone pulegenic acid ester, 154
d-cis-Cineronyl-*d*-transchrysanthemate, 154
l- cis-Cineronyl-*d*-transchrysanthemate, 154
d-cis-Cineronyl-*l*-transchrysanthemate, 154
l-cis-Cineronyl-*l*-transchrysanthemate, 154
Cinnamic acid, propyl ester, 155
Circosolv, 186
Clay loam, 170
Clothing impregnants vs. chiggers (Trombiculids), 38
CMU, 12
Coal tar derivatives, 141
Coal tar dyes, 39
Coal tar oils, 141
Cocoa butter, 149
Coconut oil, 157
Coke-oven tars, 141
Colchicine, 6
Compound 21/116, 12
Compound 21/199, 12
Compound A-42, 9
Compound 118, 2
Compound 497, 56
Compound 876, 12
Compound 923, 12
Compound 1080, 164; 172
Compound 1836, 57
Compound 2046, Shell Chem. Corp., 68
Compound 3422, 138
Copper, 170
Copper acetate, 139
Copper aceto-arsenite, 9; 139
Copper arsenate (basic), 40
Copper barium arsenate, 7
Copper chlorophenate, 140
Copper crotonoarsenite, 139
Copper cyanide, 41
Copper dichloroacetoarsenite, 139
Copper dimethyldithiocarbamate, 174
Copper 2,4-dinitro-6-cyclohexylphenate, 77
Copper fluoride, 94
Copper hydroarsenate, 7
Copper hydroarsenate-arsenite, 7
Copper-8-hydroxyquinolate, 12
Copper lauroarsenite, 139
Copper monochloroacetoarsenite, 139
Copper naphthenate, 61
Copper oleoarsenite, 139
Copper oxide, 7
Copper oxyarsenate, 40
Copper pentachlorophenate, 140; 174
Copper stearoarsenite, 139
Coramine, 93
Coriander (oil of), 149
Cork rubber sole, 170
Coumarin, 6
Coumarone, 141
Cowhide, 170
"Cracked" gasolines (gasolenes), 141
Crag Fly Repellent, 22
Creosols, 141
Creosote oils, 141
Cresylic acid soaps, 141
Crotonaldehyde, 51
Croton resin, 149
Cryolite, 42
Crystal violet, 39
CS-708, 12
Cubé, 115; 157
Cumenes, 141
Cuminic aldehyde, 104
Cunilate, 12
Cupric meta-arsenate, 7
Cupric meta-arsenite, 7
Cupric metarsenate, 7
Cupric metarsenite, 7
Cupric oxide, 139
Cyanoethylene, 1
Cyanogas®, 26
Cyclethrin, 43
1,2-Cyclohexane dicarboxylic acid, diethyl ester, 155
Cyclohexanol, chrysanthemic acid ester of, 3
Cyclohexenylallyl-acetonitrile, 1
2-Cyclohexyl-4,6-dinitrophenol, 77
dl-α-Cyclohexyl pyrrolidine, 130
l-α-Cyclohexyl pyrrolidine, 130
α-Cyclohexyl pyrroline, 130
Cyclohexyl thiocyanoacetate, 106
dl-2-(2-Cyclopentenyl)-3-methyl-2-cyclopenten-4-ol-1-onyl *dl*-cis-transchrysanthemate, 43
dl-Cyclopentenylrethronyl *dl*-cis-transchrysanthemate, 3; 43
Cysteine, 132
Cytochrome-C, 134
Cytochrome oxidase, 44

D

Dacron, 170
Dalmatian Insect Flowers, 154
Daxad #21, 9
DCPC, 54
DCPM, 15
D-D®, 45
DDD, 16; 174
DD Mixture, 45
DDT, 17; 174
p,p'-DDT, 17

Note: The numbers following the entries indicate the Section in which the entry occurs.

"DDVP", 71
Decahydro-2-naphthyl thiocyanoacetate, 106; 135
Decamethyl triphosphoramide, 132
Decane, 104
Decyl thiocyanate, 23
n-Decyl thiocyanate, 111
Decyl thiocyanate (secondary), 126
Deguelin, 46, 157
l-Deguelin, 157
"Dehydrochlorinated DDT", 17
Dehydrorotenone, 157
Demeton, 59; 172
Derrin, 157
Derris, 46; 157
Derritol, 157
DFDT, 19; 174
Diacetyl monomethoxime, 104
Diacetyl pinoresinol, 160; 171
O,O-Dialkyl S-alkyl thiomethyl phosphorodithioates, 172
Dialkyl phosphoric acid(s), 134
Dialkyl thiophosphoric esters, compounds of, with thioglycol ethers, 172
Diallyl adipate, 46
Diallyl fumarate, 103
1,5-Di-(p-N-allyl-N-methylamino) phenylpentan-3-one, 134
Diallyl succinate, 103
4,4'-Diaminodiphenyl, 126
3,3'-Diaminodiphenyl sulfone, 126
N,N'-Diamylsuccinamic acid, propyl ester, 134
Dianisyl trichloroethane, 12
2,2-Dianisyl-1,1,1-trichloroethane, 120
2,2-Di-p-anisyl-1,1,1-trichloroethane, 120
Diazinon, 61
Diazoaminobenzene, 126
p-Dibenzodioxin, 142
Dibenzothiazine, 142
Dibenzo-1,4-thiazine, 142
Dibenzothiophene, 142
Dibenzoylmethane, 126
Dibenzyl, 142
Dibenzylamine, 126
Dibenzyl ether, 126
Dibenzylketone, 126
1,1-Dibromo-2,2-bis(p-bromophenyl) ethane, 17
1,1-Dibromo-2,2-bis(p-chlorophenyl) ethane, 17
1,2-Dibromo-butane, 82; 104
α,β-Dibromoethane, 87
1,2-Dibromoethane, 87
Dibromoethane (symmetric), 87
Di-(p-bromophenyl)-trifluoromethyl carbinol, 135
1,2-Dibromo-propane, 82; 104
1,3-Dibromo-propane, 82; 104
N,N Dibutylacetoacetamide, 91
Dibutyl adipate, 47
Di-n-butyl adipate, 47
Di-sec.-butyl fluorophosphate, 134
Dibutyl phthalate, 48
Di-n-butyl phthalate, 48
N,N-Dibutyl piperonylamine, 171
S-(1,2-Dicarbethoxyethyl) O,O-dimethyl dithiophosphate, 117
S-(1,2-Dicarbethoxyethyl) O,O-dimethyl phosphorodithioate, 117
Di-p-chloraniline trichloroethane, 17
p-Dichlorbenzene, 49
Dichlor-diphenyl-dichlorethylene, 17
Dichlor-diphenyl-dichloroethane, 17
Dichlor-diphenylethane, 17
Dichlorethylene (cis), 104
Dichlorethylene (trans), 104
Di-Chloricide, 49
Dichloroacetic acid, 157
Dichloroacetonitrile, 184
2,2-Dichloroacetonitrile, 1
4,4'-Dichloroazobenzene, 126
o-Dichlorobenzene, 49
p-Dichlorobenzene, 49
4,4'-Dichlorobenzilic acid, ethyl ester, 85
4,4'Dichlorobenzohydrol, 17
4,4'-Dichlorobenzophenone, 17
p,p'-Dichlorobenzophenone, 17
2,4-Dichlorobenzyl cyanide, 1
3,4-Dichlorobenzyl cyanide, 1
1,1-Dichloro-2,2-bis-(p-bromophenyl) ethylene, 17
1,1-Dichloro-2,2-bis-(p-chlorophenyl) ethane, 17
1,1-Dichloro-2,2-bis-(p-chlorophenyl) ethylene, 17
1,1-Dichloro-2,2-bis-(p-ethylphenyl) ethane, 50
1,4-Dichlorobutane, 97
1,4-Dichloro-2-butane, 82; 104
2,2-Dichlorobutyronitrile, 1
1,1-Dichloro-2-(p-chlorophenyl)-2-(o-chlorophenyl) ethane, 17
3,3'-Dichloro-4,4'-dihydroxy diphenyl sulfone, 126
5,5'-Dichloro-2,2'-dihydroxy diphenyl sulfone, 126
Dichlorodiphenyldichloroethane, 16
Dichlorodiphenyldichlorethylene, 16
Dichlorodiphenylethane, 16
1,1-Dichloro-2,2-diphenyl ethylene, 17
o,p'-Dichlorodiphenyl methane, 17
Dichlorodiphenyl sulfide, 31
p,p'-Dichlorodiphenyl sulfide, 17
4,4'-Dichlorodiphenyl sulfone, 126
p,p'-Dichlorodiphenyl sulfone, 17
p,p'-Dichlorodiphenyl sulfoxide, 17
Dichlorodiphenyltrichloroethane, 17
Dichloroethane, 176
Dichloroethane (symmetric), 88
α,β-Dichloroethane, 88
1,2-Dichloroethane, 88
Dichloroethyl ether, 51
Dichloroethyl ether (symmetric), 51
α,β-Dichloroethyl ether, 82
β,β'-Dichloroethyl ether, 51
2,2'-Dichloroethyl ether, 51
2,3-Dichloroisobutyronitrile, 1
Dichloromethane, 123
4,4'-Dichloro-α-methylbenzhydrol, 54
4,4'-Dichloro-α-methylbenzohydrol, 54
sym.-Dichloromethyl ether, 104
Dichloronitroethane, 52
1,1-Dichloro-1-nitroethane, 52
2-(2', 4'-Dichlorophenoxy)-ethanol, 140
(Di-4-chlorophenoxy) methane, 15
4-(2,5-Dichlorophenylazo)-m-cresol, 10
4-(2,5-Dichlorophenylazo)-o-cresol, 10
p-(2,5-Dichlorophenylazo)-o-cyclohexylphenol, 10
4-(2,5-Dichlorophenylazo)-3-ethoxyphenol, 10
p-(2,5-Dichlorophenylazo)-phenol, 10
4-(2,5-Dichlorophenylazo)-resorcinol, 10
4-(2,5-Dichlorophenylazo)-2,5-xylenol, 10
2,4-Dichlorophenyl benzene sulfonate, 53
Di-(p-chlorophenyl)-n-butyl carbinol, 54
Di-(p-chlorophenyl)-dichloromethyl carbinol, 136
Di-(p-chlorophenyl) ethanol, 54
Di-(p-chlorophenyl) ether, 15; 54
Di-(p-chlorophenyl)-heptafluoropropyl carbinol, 136
Di-(p-chlorophenyl) methyl carbinol, 54
Di-(p-chlorophenyl)-pentafluoroethyl carbinol, 136
2,4-Dichlorophenyl potassium monochloroacetaldehyde sulfonate, 174
N-(3,4-Dichlorophenyl)-N'-2-(2-sulfo-4-chlorophenoxy)-5-chlorophenyl urea, Sodium salt, 127
Di-(p-chlorophenyl)-trichloromethyl carbinol, 136
Di-(p-chlorophenyl)-trifluoromethyl carbinol, 136
1,2-Dichloropropane, 150
2,2-Dichloropropane, 45
α,β-Dichloropropane, 150
2,3-Dichloropropene-1, 97
1,3-Dichloropropene + 1,2-Dichloropropane, 45
2,2-Dichloropropionitrile, 1
p,p'-Dichlorotolane, 16
Dicophane, 17
Dicoumarol, 110; 148
m-Dicyanobenzene, 1
o-Dicyanobenzene, 1
Dicyclohexylamine salt of 4,6-dinitro-o-cyclohexylphenol, 55
Dicyclohexylamine salt of DNOCHP, 55
Dicyclohexylammonium 4,6-dinitro-o-cyclohexylphenate, 55
Dicyclohexyl fluorophosphate, 134
Dicyclopentamethylene thiuram disulfide, 126
Dicyclopentamethylene thiuram hexasulfide, 126
Dicyclopentamethylene thiuram monosulfide, 126
Didakene, 177
Di-(1,3-dimethyl-n-butyl) fluorophosphate, 134
Dieldrin, 56; 174
Diesel oils, 141
3-(Diethoxyphosphinyloxy)-N-methyl-quinolinium methyl sulfate, 134
Diethoxythiophosphoric acid ester of 2-ethylmercaptoethanol, 59
Diethyl acetyl phosphate, 100; 126, 134
Diethyl adipate, 46
Diethylamine diethyl dithiocarbamate, 126
Diethylaminoethanol, chrysanthemic acid ester of, 3
Diethyl p-aminophenyl thiophosphate HCl, 134
Diethyl anilido phosphate, 134
Diethyl aryl orthophosphates (compound group), 134
Diethyl aryl phosphates: H-, p-CH_3-, p-$(CH_3)_3C$-, o-Cl-, p-Cl-, o-NO_2, p-NO_2, 2,4-di NO_2-,
Diethyl aryl phosphates: *(Continued)*
  2-NO_2-, 4-Cl, 137
Diethyl aryl thionophosphates (compound group), 134
Diethyl barbituric acid, 134
Diethyl benzene thiophosphonate, 134
Diethyl benzoyl phosphate, 134
Diethyl bis-(dimethylamino) pyrophosphate (sym. and unsym.), 172
O,O-Diethyl-O-n-butylmercaptoethyl thiophosphate, 172
Diethyl m-tert.-butylphenyl phosphate, 134
Diethyl p-tert.-butylphenyl phosphate, 134
O,O-Diethyl S-carbamylethyl dithiophosphate, 134
O,O-Diethyl-O-carbethoxymethylethyl thiophosphate, 172
Diethyl 1-carbethoxyprop-1-en-2-yl phosphate, 100; 126
Diethyl carbinol, 51
O,O-Diethyl O-o-carboethoxy phosphate, 134
Diethyl p-carboxyphenyl phosphate, 134
Diethyl-2-chloro-4-nitrophenyl thiophosphate, 134
O,O-Diethyl O-2-chloro-4-nitrophenyl thiophosphate, 134
Diethyl-2-chlorophenyl phosphate, 134
Diethyl o-chlorophenyl phosphate, 134
Diethyl p-chlorophenyl phosphate, 134
O,O-Diethyl O-o-chlorophenyl phosphate, 134
O,O-Diethyl O-p-chlorophenyl phosphate, 134
Diethyl-4-chlorophenyl phosphate, 134
Diethyl p-chlorophenyl thiophosphate, 134
Diethyl chlorophosphate, 134, 137
Diethyl p-chlorotolyl phosphonate, 134
Diethyl chlorovinyl phosphate, 57
Diethyl 2-chlorovinyl phosphate, 57; 172
Diethyl p-cyanophenyl phosphate, 134
Diethyl 2,4-dichlorophenyl phosphate, 134
Diethyl di-(dimethylamido) pyrophosphate, 132
O,O-Diethyl S-2-diethylaminoethyl phosphorothiolate oxalate, 134
Diethyl m-dimethylaminophenyl phosphate, 134
Diethyl-m-dimethylaminophenyl phosphate methiodide, 134
Diethyl 2,4-dinitrophenyl phosphate, 134
Diethyl-diphenyl-trichloroethane, 17
Diethyldithiocarbamic anhydride of O,O-di-isopropyl thionophosphoric acid, 58
Diethyldithiocarbamic phosphorodithioic anhydrosulfide, O,O-di-isopropyl ester, 58
Diethylene glycol dithiocyanate, 135
Diethylene glycol thiocyanate, 135
O,O-Diethyl-O-ethylmercapto-n-butyl thiophosphate, 172
O,O-diethyl-O-2-ethylmercaptoethyl phosphonothioate, 59
O,O-Diethyl S-2-ethylmercaptoethyl phosphorothiolate methosulfate, 134
O,O-Diethyl-Se-ethylmercaptoethyl selenothiophosphate, 172
O,O-Diethyl-O-ethylmercaptoethyl thiophosphate, 172
O,O-Diethyl-O-2-(ethylmercaptoethyl) thionophosphate, 59; 172
O,O-Diethyl-O-ethylmercaptoisopropyl thiophosphate, 172
O,O-Diethyl-O-ethylmercapto-n-propyl thiophosphate, 172
Diethyl fluorophosphate, 134
Diethyl p-formylphenyl phosphate, 134
N, N'-Diethylglutaramic acid, methyl ester, 134
O,O-Diethyl-O-n-hexylmercaptoethyl thiophosphate, 172
Di-2-ethyl hexyl phthalate, 126
O,O-Diethyl-S-2-isopropylmercaptomethyl dithiophosphate, 60; 172
O,O-Diethyl-O-(2-isopropyl-6-methyl-4-pyrimidyl) phosphorothioate, 61
O,O-Diethyl O-2-isopropyl-4-methylpyrimidyl-(6)-thiophosphonate, 61
O,O-Diethyl-O-(2-keto-4-methyl-7-α',-β'-benzo-α'-pyranyl) thiophosphate, 62
Diethyl ketone, 104
O,O-Diethyl S-mercaptoacetylurea dithiophosphate, 134
Diethyl m-methoxyphenyl phosphate, 134
Diethyl p-methoxyphenyl phosphate, 134
Diethyl p-methoxyphenyl thiophosphate, 134
O,O-Diethyl O-(4-methyl-7-coumarinyl) thionophosphate, 62
Diethylmethylcoumarinyl thiophosphate, 62
Diethyl-4-methyl-7-hydroxycoumaryl phosphorothionate, 134

Note: The numbers following the entries indicate the Section in which the entry occurs.

O,O-Diethyl-Se-methylmercaptoethyl selenothiophosphate, 172
O,O-Diethyl-O-methylmercaptoethyl thiophosphate, 172
Diethyl p-methylmercatophenyl phosphate, 134
Diethyl p-methylmercaptophenyl phosphate methosulfate, 134
Diethyl p-methylphenyl phosphate, 134
Diethyl p-methylphenyl thiophosphate, 134
O,O-Diethyl O-(3-methylpyrazolyl)-(5) phosphate, 63
O,O-Diethyl O-(3-methylpyrazolyl)-(5) thiophosphate, 64
Diethyl p-methylsulfinylphenyl phosphate, 134
Diethyl p-methylsulfonylphenyl phosphate, 134
O,O-Diethyl-O-4-methylumbelliferone ester of thiophosphoric acid, 62
Diethyl monosodium phosphate, 134
Diethyl-p-nitroanilido phosphate, 134
Diethyl p-nitrobenzyl dithiophosphate, 134
Diethyl-p-nitrobenzyl thiophosphate, 134
Diethyl-2-nitro-4-chlorophenyl phosphate, 134
Diethyl-2-nitro-4-methylphenyl thiophosphate, 134
Diethyl p-nitrophenyl monothiophosphate, 138
O,O-Diethyl-O-ethylmercapto-n-propyl thiophosphate, 172
Diethyl m-nitrophenyl phosphate, 134
O,O-Diethyl-O-m-nitrophenyl phosphate, 134
O,O-Diethyl-O-o-nitrophenyl phosphate, 134
Diethyl o-nitrophenyl phosphate, 134
O,O-Diethyl O-p-nitrophenyl phosphate, 137; 172
Diethyl p-nitrophenyl phosphate, 137
O,O-Diethyl O-p-nitrophenyl phosphorothioate, 138
O,O-Diethyl O-p-nitrophenyl thiophosphate, 138
O,O-Diethyl O-p-nitrophenyl thiophosphonate, 138
Diethyl p-nitrotolyl phosphate, 134
Diethyl orthophosphoric acid, 138
Di-(p-ethylphenyl) dichloroethane, 50
Diethyl phenyl phosphate, 134
O,O-Diethyl-O-phenyl phosphate, 134
Diethyl substituted phenyl phosphates: 2,4-di NO_2, p-NO_2, o-NO_2, m-NO_2, 2,4,5-tri-Cl, 2,4,6-tri-Cl, 2,4-di-Cl, o-Cl, p-Cl, p-$\overset{+}{S}(CH_3)_2CH_3SO_4^-$, p-$SO_2CH_3$, p-$SOCH_3$, p-$SCH_3$, m-$\overset{+}{N}(CH_3)_3I^-$, m-$N(CH_3)_2$, p-CN, m-$OCH_3$, m-tert.-butyl, p-tert.-butyl, p-CH_3, H, p-CHO, p-COOH, 134
Diethyl phenyl thiophosphate, 134
O,O-Diethyl-O-phenyl thiophosphate, 134
Diethyl phosphoric acids, 172
Diethyl o-phosphoric acid, 179
Diethyl phthalate, 148
O,O-Diethyl O-piperonyl thiophosphate, 137
O,O-Diethyl S-propylmercaptomethyl dithiophosphate, 65; 172
N,N'-Diethylsuccinamic acid, 134
Diethyl thiochlorophosphate, 134
O,O-Diethyl thiophosphoric ester of 7-hydroxy-4-methylcoumarin, 62
Diethyl 2,4,5-trichlorophenyl phosphate, 134
4,4'-Difluorobenzohydrol, 17
4,4'-Difluorobenzophenone, 17
Difluoro diphenyl trichloroethane, 19
5,10-Dihydroacridine, 142
9,10-Dihydroanthracene, 142
Dihydrocinerin I, 154
Dihydrodeguelin, 157
l -Dihydrodeguelin, 157
Dihydrometanicotine, 131
Dihydropyrone, 103
Dihydrorotenone, 157
l Dihydrorotenone, 157
l -β-Dihydrorotenone, 157
Dihydrosafrole, 171
Dihydrosafrole, chloromethyl derivative, 146
Dihydrostreptomycin SO_4, 6
1,1- Di-(2-hydroxy-2,5-dichlorophenyl)-2,2,2-trichloroethane, 174
1,1- Di-(4-hydroxy-2,5-dichlorophenyl)-2,2,2-trichloroethane, 174
2,2'-Dihydroxy-5,5'-dimethyldiphenyl sulfone, 126
4,4'-Dihydroxy-2,2'-dimethyldiphenyl sulfone, 126
4,4'-Dihydroxy-3,3'-dimethyldiphenyl sulfone, 126
Di-iodomethane, 82; 104
Diisopropylamine, 104
Diisopropyl chlorophosphate, 134
Di-isopropyl fluorophosphonate, 134
O,O-Di-isopropyl S-isopropylmercaptomethyl dithiophosphate, 66; 172
Di-isopropyl p-nitrophenyl phosphate, 134
O,O-Diisopropyl O-p-nitrophenyl thiophosphate, 134
Di-isopropyl p-nitrophenyl thiophosphate, 134
Diisopropyl parathion, 138
Di-isopropyl phosphofluoridate, 20
N,N'-Di-isopropyl phosphorodiamidic fluoride, 20
N,N'-Di-isopropylsuccinamic acid, ethyl ester, 134
Dilan®, 67
Di-lead orthoarsenate, 112
Dimefox®, 18
2,3-Dimercaptopropanol, 7
Dimeric form of 4-isopropenyl-m-cresol, 102
Dimetan, 72; 172
Di-o-methoxyaniline-trichloroethane, 17
Di-p-methoxyaniline-trichloroethane, 17
Dimethoxy trichloroethane, 12
Dimethylamidoethoxy-phosphoryl-cyanide, 134
Dimethylamido triethyl pyrophosphate, 172
m-Dimethylaminophenyl diethyl phosphate, 134
Di-p-methylaniline-trichloroethane, 17
3,3'-Dimethylazobenzene, 126
4,4'-Dimethylazobenzene, 126
Dimethyl benzene orthocarboxylate, 73
Dimethyl carbamates of pyrimidine, pyridine, pyrazine, pyridazine, 153
Dimethylcarbamyl chloride, 143
O,O-Dimethyl S-carbamyl dithiophosphate, 134
O,O-Dimethyl S-carbamylethyl dithiophosphate, 134
α,α-Dimethyl-α'-carbobutoxy-dihydro-γ-pyrone, 103
2,2-Dimethyl-6-carbobutoxy-2,3-dihydro-4-pyrone, 103
Dimethyl carbomethoxypropenyl phosphate, 68
Dimethyl-1-carbomethoxy-1-propen-2-yl phosphate, 68; 172
O,O-Dimethyl-O-1-carbomethoxy -1- propen -2-yl phosphate, 172
O,O-Dimethyl O-3-chloro-4-nitrophenyl phosphorothioate, 69
O,O-Dimethyl O-3-chloro-4-nitrophenyl thionophosphate, 69
Dimethyl-2-chloronitrophenyl thiophosphate, 70
Dimethyl 3-chloro-4-nitrophenyl thiophosphate, 69
O,O-Dimethyl O-2-chloro-4-nitrophenyl thiophosphate, 70; 134
O,O-Dimethyl O-(2-chloro-4-nitrophenyl) thiophosphate, 70
O,O-Dimethyl-O-3-chloro-4-nitrophenyl thiophosphate, 69
O,O-Dimethyl S-(1,2-dicarboethoxyethyl) dithiophosphate, 117
Dimethyl 2,2-dichlorovinyl phosphate, 71
O,O-Dimethyl-O-2,2-dichlorovinyl phosphate, 71
Dimethyl diethyl pyrophosphate, 179
Dimethyl dihydroresorcinol dimethylcarbamate, 72
5,5-Dimethyldihydroresorcinol dimethylcarbamate, 72, 172
Dimethyl diisopropyl pyrophosphate, 179
Dimethyldiphenyltrichloroethane, 16
Dimethyl-diphenyl-trichloroethane, 17
Dimethyl ester of 2,2,2-trichloro-1-hydroxyethyl phosphonate, 74
O,O-Dimethyl O-2-ethylmercaptoethyl thionophosphate, 172
Dimethylhexenol, chrysanthemic acid ester of, 3
Dimethyl hydrogen phosphate, 74
Dimethyl hydrogen phosphite, 74
O,O-Dimethyl 1-hydroxy-2-trichloromethyl phosphonate, 74
2,2-Dimethyl-3-isobutylene cyclopropene-1-carboxylic acid, 154
O,O-Dimethyl S-mercaptoacetylurea dithiophosphate, 134
Dimethyl methoxycarbonylpropenyl phosphate, 68
Dimethylnaphthalenes, 141
O,O-Dimethyl O-p-nitrophenyl phosphorothioate, 125
O,O-Dimethyl O-p-nitrophenyl thionophosphate, 125
O,O-Dimethyl O-p-nitrophenyl thiophosphate, 125
O,O-Dimethyl S-(2-oxoureidoethyl) dithiophosphate, 134; 172
Dimethyl parathion, 125
3,9-Dimethylphenothiazine, 142
Dimethyl phthalate, 73; 155
Dimethyl pinoresinol, 160; 171
Dimethyl n-propyl carbinol, 104
Dimethyl tetrachlorophthalate, 174
O,O-Dimethyl thiophosphate of diethyl mercaptosuccinate, 117
Dimethylthiuram disulfide, 126
Dimethyltrichlorohydroxyethyl phosphonate, 74
O,O-Dimethyl-2,2,2-trichloro-1-hydroxyethyl phosphonate, 6; 74
Dimite®, 54
Dinex®, 77
Dinitroanisole, 111
Dinitrobutylphenol, 75
2,4-Dinitro-6-sec.-butylphenol, 75
4,6-Dinitro-2-sec.-butylphenol, 75
4,6- Dinitro-o-sec.- butylphenol, 174
Dinitrocapryl phenylcrotonate, 75
Dinitrocresol, 76
4,6-Dinitro-o-cresol, 76
2,4-Dinitro-6-cyclohexylphenol, 77
4,6-Dinitro-2-cyclohexylphenol, 77
2,4-Dinitro-6-cyclopentylphenol, 75
2,4-Dinitro-6-ethylphenol, 78
2,4-Dinitro-6-n-heptylphenol, 75
2,4-Dinitro-6-n-hexylphenol, 75
3,5-Dinitro-2-hydroxytoluene, 76
2,4-Dinitro-4'-methyldiphenyl sulfone, 126
2,4-Dinitro-3-methyl-6-isopropylphenol, 75
2,4-Dinitro-6-methylphenol, 76
4,6-Dinitro-2-methylphenol, 76
Dinitro-α-naphthol, 77
2,4-Dinitro-6-n-octylphenol, 75
3,5-Dinitro-ortho-cresol, 76
2,4-Dinitro-6-n-pentylphenol, 75
Dinitrophenols, general treatment, 78
Dinitrophenothiazine sulfoxide, 142
2,4-Dinitrophenyl chlorophenyl ether, 140
Di-(p-nitrophenyl)-p-chlorotolyl phosphate, 134
2,4-Dinitro-6-n-propylphenol, 75
Dinitro-1-trichloro-2,2-bis(p-chlorophenyl) ethane, 17
Dinitro-1-trichloro-2,2-di-p-tolylethane, 17
Dinoseb, 75
Dioctyl fumarate, 126
Dioctyl sebacate, 126
m-Dioxane, 5-butyl-5-ethyl-2 (3,4-methylene dioxyphenyl), 134
Diparcol, 130
Diphenyl, 142
Diphenyl acetyl indan(e)dione, 110; 148
Diphenyl acetyl indan(e)dione, Fe^{++} salt, 110
Diphenylamine, 111; 126; 142
Diphenyl carbinol, 54
Diphenyl carbonate, 38; 91
Diphenyl chlorothionphosphonate, 100; 126
n-Diphenyl N-diethylthiuram disulfide, 126
Diphenyl diimide, 10
Diphenyl-α, β- diketone, 38
N-Diphenyl N-dimethylthiuram disulfide, 126
Diphenyl disulfide, 126
Diphenylene oxide, 79; 142
1,1-Diphenylethane, 17
1,2-Diphenylethanedione, 38
1,1-Diphenylethylene, 17
Diphenyl ethyl thionophosphate, 100; 126
Diphenyl fluorophosphate, 134
α,γ-Diphenyl glycerol, 126
1,1-Diphenyl-(4-hydroxy-3,5-dichloro)-2,2,2-trichloroethane, 174
Diphenyl mercury, 174
Diphenylmethane, 17; 142
Diphenyl selenium, 174
Diphenyl sulfide, 126
Diphenyl sulfone, 80
Diphenyl sulfoxide, 142
Diphenyltrichloroethane, 16
2,2'-Dipiperidyl, 131
2,3'-Dipiperidyl, 131
3,3'-Dipiperidyl, 131
3,4'-Dipiperidyl, 131
4,4'-Dipiperidyl, 131
Diplumbic hydrogen arsenate, 112
Dipropyl adipate, 46
Di-n propyl maleate-isosafrole condensate, 152
Di-n-propyl-2-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydronaphthalene-3,4-dicarboxylate, 152
Di-propyl p-nitrophenyl thiophosphate, 134
Di-n-propyl p-nitrophenyl thiophosphate, 134
N, N'-Dipropylsuccinamic acid, ethyl ester, 134
Dipterex®, 74
2,2'-Dipyridyl, 131
2,3-Dipyridyl, 130, 131
3,3'-Dipyridyl, 131

Note: The numbers following the entries indicate the Section in which the entry occurs.

3,4'-Dipyridyl, 131
4,4'-Dipyridyl, 131
Disaccharides, 154
Disodium p-nitrophenyl phosphate, 134
"Distillate", 141
β,β' - Di-(α-tetrahydrofurfuryl) diethyl carbinyl thiocyanoacetate, 106
β,β' - Di-(α-tetrahydrofuryl) diethyl carbinyl thiocyanocaetate, 135
β,β' -Dithiocyanoethyl ether, 82
Dithione, 178
Dithionopyrophosphates (compound group), 134
Dithiophosphates (compound group), 134
DMC, 54; 171
DMDT, 120
DMP, 73
DN, 76
DN-111, 55
DNBP, 75
DNC, 76
DNOC, 76
DNOCHP, 77
DNOC phenyl mercury, 76
DNOSBP, 75
DNSBP, 75
DNTP, 138
Dodecamethyl tetraphosphoramide, 132
Dodecyl nicotinium bromide, 130
Dodecyl nicotinium dibromide, 130
Dodecyl nicotinium diiodide, 130
Dodecyl nicotinium iodide, 130
Dodecyl pentachlorophenyl ether, 140
Dodecyl thiocyanate, 23; 111
Dodecyl thiocyanate (secondary), 126
n-Dodecyl thiocyanate (= Lauryl thiocyanate), 111
Dormant oils, 141
Dowfume EB-5, 88
Dowfume W-10, 87
Dowfume W-40, 87
Dowicide 7, 140
DPP, 138
DPS, 80
Dry Mix No. 1 (Dow Chemical Company), 77
Duponol WA Powder, 9
Dutch liquid, 88
Dynone II, 55

E

E-393, 178
E-600, 137
E-605, 138
E-838, 62
E-1059, 59
E-3314, 96
E-8573, 180
Eau Grison, 113
EDB, 87
Elemental phosphorus, 144
Elliptone, 46; 157
l-Elliptone, 157
EMCOL H 65 A, 156
Enanthoyl indanedione, 110
Endrin, 81
1,1,2,2,3,4,4,5,6-Enneachlorocyclohexane, 13
Ephedrine, 159
Epibromohydrin, 82; 104
Epichlorohydrin, 82
EPN®, 93
1,2-Epoxyethane, 89
1,2-Epoxypropane, 151
Esters, 154
Ethanol, 104
Ethanol, 2-phenoxy-, acetate, 155
2-Ethanol-pyridine, 104
Ethanol, 2,2'-thiodi-,diacetate, 155
Ethers, 154
Ethide®, 52
Ethinyl trichloride, 186
Ethohexadiol, 91
2-(2-Ethoxyethoxy)-ethyl thiocyanoacetate, 106; 135
Ethoxymethyl dichlorophenyl carbinol, 83
Ethoxymethyl di-(p-chlorophenyl) carbinol, 83
1-Ethoxymethyl-1,1-di-(p-chlorophenyl) carbinol, 83
Ethyl acetate, 84
Ethyl acrylate, 103; 104
S-Ethyl O,O-bis(p-nitrophenyl) thiophosphate, 138
Ethyl bromoacetate, 82
Ethyl-1-bromopropionate, 104
2-Ethylbutylimide of endomethylene tetrahydrophthalic, 92
Ethylbutyl p-nitrophenyl thiophosphate, 134
Ethyl butyrate, 134, 179
Ethyl caproate, 104
Ethyl carbamate, 6
Ethyl carbanilate, 6
O-Ethyl-O-p-carboethoxy methane phosphonate, 134
Ethyl chloroacetate, 104
O-Ethyl-O-o-chlorophenyl methane phosphonate, 134
Ethyl-4,4'-dichlorobenzilate, 85
Ethyl-4,4'-dichlorodiphenyl glycollate, 85
Ethyl di-(dimethylamido) phosphate, 132
O-Ethyl-N (dimethylamido)-O-p-nitrophenyl, phosphate, 134
Ethyl disulfide, 104
Ethylene bromide, 87
Ethylene chloride, 88
Ethylene chlorobromide, 86
Ethylene chlorohydrin, 51; 104
Ethylene dibromide, 87
Ethylene dichloride, 88
Ethylene glycol ether of pinene, 171
Ethylene oxide, 89
Ethylene tetrachloride, 177
Ethylene trichloride, 186
Ethyl formate, 90
Ethyl hexanediol, 91
2-Ethyl-1,3-hexanediol, 91; 155
N-(2-Ethylhexyl)-bicyclo- [2.2.1] -5-heptene-2,3-dicarboximide, 92; 171
Ethyl hexylene glycol, 91
N-2-Ethylhexylimide of endomethylene tetrahydrophthalic acid, 92
2 - Ethylhexyl - 3,4 - methylenedioxyphenyl ether, 171
2-Ethylhexyl thiocyanoacetate, 106
Ethylidene chloride, 104
Ethyl isobutyrate, 104
Ethyl isothiocyanate, 23
Ethyl mercaptan, 82
Ethylmercaptoethyl diethyl thiophosphate, 59
O-Ethyl-2-mercaptoethyl phosphate, 59
2-Ethyl-6-methyl-pyridine, 104
Ethyl monochloroacetate, 104
Ethyl nitrite, 104
O-Ethyl-O-2-nitro-4-methylphenyl methane phosphonate, 134
Ethyl-p-nitrophenyl benzenethionophosphate, 93
O-Ethyl-O-o-nitrophenyl methane phosphonate, 134
O-Ethyl-O-p-nitrophenyl phenylphosphonothioate, 93
Ethyl-p-nitrophenyl thiobenzene phosphonate, 93
Ethyl-p-nitrophenyl thionobenzene phosphonate, 93
O-Ethyl O-o-nitrophenyl thionobenzene phosphonate, 134
Ethyl orthoformate, 104
Ethyl pentachlorophenoxyacetate, 140
N-Ethylphenothiazine, 142
6-Ethylphenothiazine, 142
Ethylphenylacetate, 104
Ethylphenyl-hydroxy-trichloroethane, 17
O-Ethyl O-phenylmethane phosphonate, 134
2-Ethyl 3-propyl-1,3-propanediol, 91
2-Ethyl-pyridine, 104
4-Ethyl-pyridine, 104
O-Ethyl-2-sulfinylethyl phosphate, 59
S-Ethyl-2-sulfinylethyl phosphorothiolate, 59
O-Ethyl-2-sulfinylethyl phosphorothionate, 59
O-Ethyl-2-sulfonylethyl phosphate, 59
S-Ethyl-2-sulfonylethyl phosphorothiolate, 59
O-Ethyl-2-sulfonylethyl phosphorothionate, 59
Ethyl tetrachlorophenoxyethyl acetate, 140
Ethyl thiocyanate, 23, 104
Ethyl thiocyanofumarate, 106; 135
Ethyl β-thiocyanopropionate, 135
Ethyl thiodichlorophosphate, 134
O-Ethyl-2-thioethylethyl thionophosphate, 12
Etoxinol, 83
Eudesamin, 160; 171
Eugenol, chrysanthemic acid ester of, 3
Experimental Insecticide 711 (Julius Hyman Company), 108
Experimental Insecticide 4049 (American Cyanamid Company), 117
Experimental Insecticide 4124 (American Cyanamid Company), 70
Experimental Miticide 7, 22
Experimental Tick Repellents 3 and 3 PS, 47

F

Fagaramide, 171
Fagarimide, 107
2-Fenchoxyethyl thiocyanoacetate, 106; 135
Fenchyl thiocyanoacetate, 106; 135
Fermate, 174
Ferric arsenate, 7
Ferric dimethyldithiocarbamate, 174
Ferrous arsenate, 7
Fish oil green (Paris green homologue), 139
Fleck-Flip, 186
Flour sulfur, 168
Flowers of sulfur, 168
Fluoaluminates, 94
Fluorene, 141
Fluorides, 94
Fluorine, 94
Fluorobenzene, 104
Fluoro-DDT, 19
Fluoroethoxymethane, 18
Fluoroethyl alcohol, 18
Fluorogesarol, 19
Fluorophosphine oxide, 18
o-Fluorotoluene, 104
Fluosilicates, 94
Formaldehyde, 111
Formic acid, 104
Fosvex, 179
French Green, 139
Fuel oils, 141
Fumette, 119
Furethrin, 95
Furfurylcarbinol, chrysanthemic acid ester of, 3
dl-2-(2-Furfuryl-4-hydroxy-3-methyl-2-cyclopenten-1-one ester of *dl*-cis-trans-chrysanthemum monocarboxylic acid, 95
dl-2-(2-Furfuryl)-3-methyl-2-cyclopenten-4-ol-1-onyl *dl*-cis-trans-chrysanthemate, 95
dl-Furfurylrethronyl *dl*-cis-trans-chrysanthemate, 95
Furoyl chloride, 104
FW-152, 16

G

G-338, 85
G-19258, 72; 143
G-22007, 143
G-22008, 143
G-22417, 143
G-22418, 143
G-22868, 143
G-22869, 143
G-22870, 143
G-22872, 143
G-22873, 143
G-22890, 143
G-22955, 143
G-22972, 143
G-23007, 143
G-23008, 143
G-23012, 143
G-23015, 143
G-23027, 64
G-23162, 143
G-23165, 143
G-23224, 143
G-23234, 143
G-23235, 143
G-23236, 143
G-23323, 143
G-23327, 143
G-23328, 143
G-23330, 153
G-23611, 109
G-23612, 143
G-23613, 143
G-23629, 143
G 23645, 83
G-23841, 143
G-23842, 143
G-23883, 143

Note: The numbers following the entries indicate the Section in which the entry occurs.

G-23884, 143
G-23890, 143
G-23897, 143
G 23992, 85
G-24041, 143
G-24080, 143
G-24151, 143
G-24152, 143
G-24344, 143
G-24480, 61
G-24483, 63
Gamma-isomer of benzene hexachloride, 114
Gamma-isomer of hexachlorocyclohexane, 114
Gammexane, 114
Gamoxo, 114
Gamtox, 114
Gas oils, 141
Gasoline (= Gasolene), 104
Gasolines, 141
Gemalgene, 186
Genicide acids, 174
Geniphene, 183
Genite®, 53
Genite 923 of Allied Chemical and Dye Corporation, 53
Genithion, 138
Germalgene, 186
Germerine, 159
Germidine, 159
Germine, 159
Germitrine, 159
Gesarol, 17
"Gix", 19
Glucuronic acid, 138
Gmelinol, 160
Grapefruit seed oil, 157
Ground Rock Sulfur, 168
Ground tobacco, 170
Guaiacol, chrysanthemic acid ester of, 3
Gypsine, 112

H

Halogenophosphates (compound group), 134
Hanane, 18
Hardwood flour, 170
Heavy summer oils, 141
Heliotropine, 149
HEOD, 56
Heptachlor, 96
Heptachlor (epoxide of), 96
1,2,3,4,5,7,7-Heptachlorobicyclo- [2,2,1] -2-heptene, 108
Heptachlorocyclohexane, 13
α-Heptachlorocyclohexane, 13
β-Heptachlorocyclohexane, 13
3,4,5,6,7,8,8a-Heptachlorodicyclopentadiene, 96
Heptachloropropane, 97
1,4,5,6,7,8,8-Heptachloro-3a,4,7,7a-tetrahydro-4,7-endomethanoindene, 96
Heptachlorotetrahydro-4,7-methanoindane, 96
2-Heptadecyl glyoxalidine acetate, 126
Heptamethyl pyrophosphoramide, 132
Heptane, 154
2-n-Heptyl-pyridine, 104
sec.-Heptyl thiocyanate, 126
Herculin, 107; 171
HETP, 100
1,2,3,4,5,6-Hexabromocyclohexane, 13
1,2,3,4,5,6-Hexachlorocyclohexane, 13
γ-1,2,3,4,5,6-Hexachlorocyclohexane, 114
Hexachlorocyclopentadiene, 108
1:2:3:4:11:11: Hexachloro-6:7-epoxy-1:4:5:6:7:8:9:10-octahydro-1:4:5: 8-diendomethylenenaphthalene, 56
Hexachloro-epoxy-octahydro-dimethanonaphthalene, 56
1,2,3,4,10,10-Hexachloro-6,7-epoxy-1,4,4a,5,6,7, 8,8a-octahydro-1,4,5,8-dimethanonaphthalene, 56
1,2,3,4,10,10-Hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-endo, endo-5,8-dimethanonaphthalene, 81
1,2,3,4,10,10-Hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-endo, exo-5,8-dimethanonaphthalene, 56
Hexachloroethane, 98
1,1,1,2,2,2-Hexachloroethane, 98
1,2,3,4,10,10-Hexachloro-1,4,4a,5,8,8a-hexahydro-1, 4-endo, endo-5,8-dimethanonaphthalene, 108
1,2,3,4,10,10-Hexachloro-1,4,4a,5,8,8a-hexahydro-1, 4-endo, exo-5,8-dimethanonaphthalene, 2
Hexachlorooctahydro-endo, endo-dimethanonaphthalene, 81
Hexachlorophenol, 140; 174
Hexachloropropene, 99
α,α'-Hexachloro-m-xylene, 17
α,α'-Hexachloro-o-xylene, 17
α,α'-Hexachloro-p-xylene, 17
Hexadecyl thiocyanate, 23
n-Hexadecyl thiocyanate (=Cetyl thiocyanate), 111
Hexadow, 114
"Hexaethyl tetraphosphate", 100; 126
Hexaethyl tetraphosphate esters: Hexabutyl, Hexaethyl, Hexa-(2-ethylhexyl), Hexapropyl, 134
Hexahydrobenzoyl indanedione, 110
Hexahydrophthalic acid, di-n-butyl ester, 134
Hexamite, 179
Hexane, 154
Hexone, 114
Hexyl mandelate, 91
3-Hexyl-5-(3,4-methylenedioxyphenyl)-2-cyclohexene-1-one, 147
3-n-Hexyl-5-(3,4-methylenedioxyphenyl)-2-cyclohexenone + its 6-carbethoxy- derivative, 147
2-Hexyl-6-methyl-pyridine, 104
n-Hexyl pentachlorophenyl ether, 140
2-n-Hexyl-piperidine, 104
2-n-Hexyl-pyridine, 104
4-mixed-Hexyl-pyridine, 104
4-n-Hexyl-pyridine, 104
n-Hexyl thiocyanate, 111
sec.-Hexyl thiocyanate, 126
n-Hexyl thiocyanoacetate, 106
HHDN, 2
Hinokinin, 160
Holcomb Compound 326, 58
Horsehide, 170
Hydracrylic acid, β-phenylethyl ester, 155
Hydrazobenzene, 126
4-Hydrazobenzene, 126
Hydrocarbons (10-16 carbons), 141
Hydrocarbons (14-18 carbons), 141
Hydrocyanic acid, 101
Hydrocyanic acid gas, 101
Hydrogen cyanide, 101
Hydrogen selenide, 166
Hydroquinone, 142; 154
4-Hydroxyazobenzene, 126
Hydroxylamine, 132
3-Hydroxymethyl-n-heptan-4-ol, 91
3-Hydroxy-8-nonene-2,5-dione *d*-trans-chrysanthemate, 3
Hydroxypentamethyl flavan, 102
2'-Hydroxy-2,4,4,7,4'-pentamethyl flavan, 102
Hydroxyrotenone, 157

I

Imperial Green, 139
IN 930, 107
Indalone®, 103; 155
1,3-Indandiones, 148
Indanedione (non-acylated), 110
Indene, 141
Insecticidal fumigants; general considerations, comparative tables, data, 104
Insecticide sprays, behavior of droplets of different sizes, 105
612 Insect repellent, 91
Iodoacetic acid, 132
p-Iodobenzene, 10
1-Iodo-butane, 82; 104
2-Iodo-butane, 82; 104
Iodo-cyclohexane, 82; 104
Iodoethane, 82; 104
1-Iodo-heptane, 82; 104
1-Iodo-hexane, 82; 104
1-Iodo-3-methyl butane, 82; 104
1-Iodo-2-methyl-propane, 82; 104
Iodonaphthalene, 129
1-Iodo-pentane, 82; 104
4-(p-Iodophenylazo)-o-cresol, 10
1-Iodo-propane, 82; 104
3-Iodo-propene, 82; 104
Iron (Fe^{++}) salt of diphenylacetyl indandione, 148
Iron (Fe^{++}) salt of 2-isovaleryl-1,3-indandione, 148
Iron (Fe^{++}) salt of 2-pivalyl-1,3,indandione, 148
Isoamyl formate, 104
Isoamyl mercaptan, 104
(3-Isoamyl-5-methylenedioxyphenyl)-2-cyclohexenone, 147
Isoamyl nitrite, 104
Isobornyl thiocyanoacetate, 106
Isobrom D, 87
Isobutenyl chloride, 121
Isobutyl acetate, 104
Isobutylamide of undecylenic acid, 107
Isobutylamides of unsaturated aliphatic acids, 171
Isobutylamine, 104
Isobutyl benzoate, 104
Iso-butyl bromide, 104
N-Isobutyl-2,4-decadienamide, 107; 171
N-Isobutyl-2,6-decadienamide, 107; 171
N-Isobutyl-4,6-decadienamide, 107; 171
N-Isobutyl-2,6,8-decatrienamide, 107; 171
N-Isobutyl-2,8-dodecadienamide, 107; 171
N-Isobutyl-2-dodeceneamide, 107; 171
Isobutyl formate, 104
N-Isobutyl hendecenamide, 107
Isobutyl indanedione, 110
Isobutyl iodide, 104
N-Isobutyl lauramide, 107; 171
Isobutyl mercaptan, 104
N-Isobutyl-3,4- methylenedioxicinnamide, 171
N-Isobutyl-2,4,8,10,14-octadecapentaenamide, 107, 171
N-Isobutyl-2,4,8,12,14-octadecapentaenamide, 107, 171
N-Isobutyl undecyleneamide, 107; 171
Iso-butyl valerate, 104
Isobutyraldehyde, 104
Isobutyronitrile, 1
Isocapronitrile, 104
Isocrotyl bromide, 97
Isocrotyl chloride, 97
Iso-DDT, 17
Isodrin, 108
Isogmelinol, 160
Isohydrocinerin I, 154
Isohydrocinerin II, 154
Isohydropyrethrin I, 154
Isohydropyrethrin II, 154
Isolan, 109; 172
Isonicoteine, 130
Isoparaffin (heavy), 141
Iso-pentane, 104
Isopestox®, 20; 172
Isopropanol, 104
Isopropyl bromide, 104
Isopropyl ether, 104
Isopropyl formate, 104
Isopropyl iodide, 104
Isopropylmethylpyrazolyl dimethylcarbamate, 109
1-(Isopropyl-3-methylpyrazolyl-(5)-dimethylcarbamate, 109; 172
O,2-Isopropyl-4-methylpyrimidyl-O,O-diethyl phosphorothioate, 61
Isopropylmethylpyrimidyl diethyl thiophosphate, 61
Isopropyl monochloroacetate, 104
2-Isopropyl-pyridine, 104
4-Isopropyl-pyridine, 104
Isopropyl thiocyanate, 82
Isoquinoline, 131
Iso-rotenone, 157
Iso-rubijervine, 159
Isosafrole, 171
Isosesamin, 160, 171
Isotex, 114
Isothiocyanates: Allyl, Ethyl, 135
Isothiocyanic acid, ethyl ester, 82
Isovaleryl indandione, 110
2-Isovaleryl-1,3-indandione, 110; 148; 171
2-Isovaleryl-1, 3-indanedione, 171
Isovaleryl indanedione, Cu^{+} salt, 110
Isovaleryl indanedione, Cu^{++} Salt, 110
Isovaleryl indanedione, Fe^{++} salt, 110
2-Isovaleryl-1,3-indanedione sodium, 6

J

Jervine, 159

K

K-1875,15
K-6451,35

Note: The numbers following the entries indicate the Section in which the entry occurs.

Kerosene (heavy), 141
Kerosene (light), 141
Kerosenes, 141
Kutira gum, 149

L

Lactic acid, 164
Lanadin, 186
Lauryl rhodanate, 111
Lauryl thiocyanate, 111
Lauseto Neu, 33
Lead arsenate, 112
Lead 2,4-dinitro-6-cyclohexylphenate, 77
Lead fluoride, 42
Lead oxide, 7
Lead tetraacetate, 158
Lethane 60®, 135, 182
Lethane A-70®, 23
Lethane B- 71a®, 23
Lethane B-72®, 23
Lethane 384®, 23, 135
"Lethanes", 23
Lethane Special®, 135
Lethurin, 186
Leucophenothiazone, 142
Leucothionol, 142
Lewisite, 7
"Light" oils, 141
Lime-sulfur, 113
Lime-sulphur, 113
Lindane, 114; 174
Linseed oil, 157
Linseed oil green (Paris green homologue), 139
Lonchocarpic acid, 157
Lonchocarpus, 115; 157
London purple, 7
Loro®, 111; 135
Lorol-2-thiazolinyl sulfide, 126
"Lube" oils, 141
Lubricating oils, 141
Lupinine, 5
Lutidine, 131
Lutidines, 141
Lysol, 111

M

M-2020, 91
Magnesium arsenate, 116
Magnesium 2,4-dinitro-6-cyclohexylphenate, 77
Magnesium fluoride, 94
Magnesium oxide, 7
Malaccol, 46; 157
Malachite green, 39
Malathion, 117
Malathon (formerly), 117
Malonic acid, 132
Manganese fluoride, 42
Marlate® 50, 120
Marlate® 2-MR, 120
Me 1700 [I. G. Farbenindustrie A. G.], 16
Medicinal mineral oils, 141
"Medium" oils, 141
Medium summer oils, 141
Menadione, 6
Menthol, chrysanthemic acid ester of, 3
Mephyton, 148
S-Mercaptoacetylurea O,O-diethyl dithiophosphate, 134
S-Mercaptoacetylurea O,O-dimethyl dithiophosphate, 134
Mercaptobenzothiazole, 141
2-Mercapto-6-nitrobenzothiazole, 16
Mercurated pentaethyl triphosphate (and related phosphates), 126
Mercurous chloride, 118
Mercury nono-, proto-, or subchloride, 118
Mesitylene, 104
Mesityl oxide, 103
2-Mesityl-α-pyrrolidine, 130
2-Mesityl-α-pyrroline, 130
Metacide®, 125
Metanicotine, 131
Meta-Systox®, 172
Methane sulfonyl fluoride, 119
Methionine, 166
Methoxychlor, 120, 174
Methoxy-DDT, 120
2-Methoxyethyl-3, 4-methylenedioxyphenyl-acetal-acetal-dehyde, 171
2-Methoxyethyl thiocyanoacetate, 106; 135
β-Methylallyl chloride, 121
Methylallylrethronlyl *d*-trans-chrysanthemate, 3
Methyl N-amyl ketone, 126
N-Methylanabasine, 130
Methyl analogue of parathion, 125
l-N-Methylanatabine, 130
β - Methylanthraquinone, 174
4-Methylazobenzene, 126
Methyl benzoate, 157
Methyl bromide, 122
Methyl bromoacetate, 82
Methyl butyl carbinol, 104
Methyl n-butyl ketone, 104
Methyl n-butyrate, 104
Methyl caprylate, 104
Methyl chloroacetate, 104
Methyl chlorocarbonate, 104
Methyl chloroform, 185
Methyl cyanide, 51
4-Methyl cyclohexanol, 157
Methylcyclohexanol, chrysanthemic acid ester of, 3
1-Methyl-3-cyclohexyl-n-propyl thiocyanoacetate, 106; 135
Methyl-N,N'-di-isopropyl adipamate, 91
Methyl disulfide, 82
Methylene bichloride, 123
Methylene chloride, 123
3,4-Methylene dioxyphenol, 160
1-(3,4-Methylenedioxyphenyl)-1-butanol, 171
4-(3,4-Methylenedioxyphenyl)-3-butene-2-one, 171
1-(3,4-Methylenedioxyphenyl)-4- phenyl -1- butanol, 171
3,4-Methylenedioxy-6-propylbenzyl butyldiethylene - glycol ether, 146
Methylene iodide, 82
Methylethyl parathion, 134
Methyl formate, 124
Methyl homologue of parathion, 125
α-Methyl hydroxylamine, 104
4-Methyl-2-hydroxythiazole, 106; 135
Methyl iodide, 82
1-Methylisobutylimide of endomethylene tetrahydrophthalic acid, 92
Methyl isobutyl ketone, 104
Methyl isopropenyl ketone, 104
p-Methylmercaptophenyl diethyl phosphate, 134
Methylmetanicotine, 131
2-Methyl-4-methyl-pyridine, 104
2-Methyl-5-methyl-pyridine, 104
2-Methyl-6-methyl-pyridine, 104
Methyl monochloroacetate, 104
Methylnaphthalenes, 141
2- Methyl-1,4-naphthoquinone, 110
Methyl nitrite, 104
O-Methyl O-o-nitrophenyl thionobenzene phosphonate, 134
2-(2-Methyloctyl)-pyridine, 104
Methyl oxiane, 151
Methyl parathion, 125
Methyl pentachlorophenyl ether, 140
N-Methyl phenothiazine, 142
6-Methyl phenothiazine, 142
Methylphenylpyrazolyl dimethylcarbamate, 143
3-Methyl-1-phenylpyrazolyl-(5)-dimethylcarbamate, 143; 172
Methyl phthalate, 73
2-Methyl-3-phytyl-1,4-naphthoquinone, 148
2-(1-Methyl-n-propyl)-4,6-dinitrophenol, 75
Methyl n-propyl ketone, 104
Methylpyrazolyl diethyl phosphate, 63
3-Methylpyrazolyl-(5)-diethyl phosphate, 63; 172
Methylpyrazolyl diethyl thiophosphate, 64
2-Methyl-pyridine, 104
3-Methyl-pyridine, 104
Methyl-3,2'-pyridylpiperidine, 131
l-1-Methyl-2-(3'-pyridyl)-pyrrolidine, 130
N-Methylpyrrolidine, 130
1-3-(1-Methyl-2-pyrrolidyl) pyridine, 130
Methyl selenide, 166
Methyl selenocyanate, 104
Methyl sulfide, 104
p-Methylsulfinyl diethyl phosphate, 134
1-Methyl-3-(α-tetrahydrofurfuryl-n-propyl thiocyanoacetate, 106
2-(1-Methyl-3- [α-tetrahydrofuryl] -n-propoxyethyl) thiocyanoacetate, 135
1-Methyl-3-(α-tetrahydrofuryl)-n-propyl thiocyanoacetate, 135
Methyl thiocyanate, 82; 135
Methyl thiocyanoacetate, 106; 135
Metrazol, 93
MGK 264®, 92
"Mike" sulfur, 170
Mild mercury chloride, 118
Mineral oils, 141
Mintacol, 137
Mipafox®, 20
Mischler's ketone, 151
Miscible oils, 141
Miticides, 126
Mitin®, 127
Monobromomethane, 122
Mono-n-butyl ether of diethylene glycol, Sodium salt, 146
Monochloroacetonitrile, 184
α-Monomethyl naphthalene, 141
β-Monomethyl naphthalene, 141
Monophosphoramide of OMPA, 132
Morphine, 138
Mosquito larvae; tests of insecticides against, 128
"Moth balls", 129
"Moth flakes", 129
M.S.F., 119
Murvesco, 34
Myristyl thiocyanate, 111

N

Naphthalene, 129, 141
Naphthalin, 129
Naphthas, 141
Naphthene, 129
Naphthenes, 141
Naphthenic oils, 141
α - Naphthoflavone, 174
2-β- Naphthoxyethyl thiocyanoacetate, 106; 135
α-Naphthoyl indanedione, 110
β- Naphthoyl indanedione, 110
α-Naphthyl thiocyanoacetate, 135
Natural rubber, 170
Neat's foot oil, 157
Neocid, 17
Neogermidine, 159
Neogermitrine, 159
Neolite sole, 170
Neomycin SO_4, 6
Neonicotine, 5
Neoprene rubber, 170
Neotran®, 15
Niagaramite, 24
Nicoteine, 130
Nicotelline, 130
Nicotiana glauca, 5
Nicotimine, 130
Nicotine, 130
Nicotine $CuCl_2$, 130
Nicotine $ZnCl_2$, 130
dl-α-Nicotine, 130
d-β- Nicotine, 130
dl-β- Nicotine, 130
l-β- Nicotine, 130
l-Nicotine acid δ-tartrate, 130
Nicotine alginate, 130
Nicotine aresket, 130
Nicotine bentonite, 130
Nicotine bitartrate, 130
Nicotine caseinate, 130
Nicotine copper ferrocyanide, 130
Nicotine cuprocyanide, 130
Nicotine 2,4-dinitro-o-cyclohexylphenate, 130
Nicotine humate, 130
Nicotine laurate, 130
Nicotine naphthenate, 130
Nicotine peat, 130
Nicotine reineckate, 130
Nicotine resorcinol-formaldehyde, 130
Nicotine silicotungstate, 130
Nicotine stannichloride, 130
Nicotine stearate, 130
Nicotine sulfate, 130
Nicotine tannate, 130
Nicotyrine, 130; 131

Note: The numbers following the entries indicate the Section in which the entry occurs.

Nicouline, 157
Nifos, 179
Nifos T, 179
Nigrosine, 164
Niran, 138
Nitriles, 1
p-Nitrobenzoic acid, 6
1-Nitrobutane, 52
2-Nitrobutane, 52
Nitrochloroform, 37
p-Nitro-m-chlorophenyl dimethylthionophosphate, 69
Nitroethane, 52
Nitromethane, 52
p-Nitrophenol, 6; 134
o-Nitrophenyl acetate, 134; 179
4-(p-Nitrophenylazo)-resorcinol, 10
p-Nitrophenyl dichlorothionphosphonite, 100; 126
p-Nitrophenyl diethyl phosphate, 100; 126
p-Nitrophenyl diethyl thionophosphate, 126
p-Nitrophenyl diethyl thionphosphate, 126
p-Nitrophenyl diisopropyl phosphate, 126
1-Nitropropane, 52
2-Nitropropane, 52
N-Nitrosocarbazole, 126
N-Nitrosodiphenylamine, 126
α,α',α''-Nonachloromesitylene, 17
2,4-Nonanediol, 91
Nonyl thiocyanate (secondary), 126
Nornicotine, 131
d-B-Nornicotine, 131
dl-B-Nornicotine, 131
l-B-Nornicotine, 131
NPD, 180
Nujol®, 141
Nylon, 170

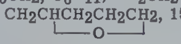
O

Octachlorocamphene, 183
Octachlorocyclohexane, 13
α-1,1,2,2,3,4,5,6-Octachlorocyclohexane, 13
β-1,1,2,2,3,4,5,6-Octachlorocyclohexane, 13
β-1,1,2,3,4,4,5,6-Octachlorocyclohexane, 13
Octachlorodihydrodicyclopentadiene, 30
1,2,4,5,6,7,8,8-Octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene, 30
1,2,4,5,6,7,8,8-Octachloro-4,7-methane-3a,4,7,7a-tetrahydroindane, 30
Octacide 264, 92
Octadecyl thiocyanate, 23
n-Octadecyl thiocyanate (= Stearyl thiocyanate), 111
Octa-Klor, 30
"Octalene", 2
Octalox, 56
Octamethyl pyrophosphoramide, 132; 172
Octamethyl pyrophosphoramide N-oxide, 132
Octamethyl tetramido pyrophosphate, 132; 134
N-Octyl bicycloheptene dicarboximide, 92
2-n-Octyl-pyridine, 104
2-(3-Octyl)-pyridine, 104
n-Octyl sulfoxide of isosafrole, 133; 171
Octyl thiocyanate, 23
n-Octyl thiocyanate, 111
Octyl thiocyanate (secondary), 126
Odorless distillate, 154
Odorless kerosene, 141
Oil of anise, 149
Oil of basil, 149
Oil of coriander, 149
Oleic acid, 154
Oleic acid salts, 141
Olivenite, 40
Olive oil, 154
OMPA, 132; 172
Organic Phosphates, 134
Organic Phosphorus Insecticides, 134
Organic thiocyanates; thiocyanoacetates, 135
"Organophosphorus Insecticides", 134
Orlon, 170
Orthophosphates (compound group), 134
Orthophosphoric acid, 137
Orthothiophosphates (compound group), 134
Oviposition inhibitors, 136
Ovotran®, 35
Oxalyl chloride, 104
Oxirane, 89
Oxoryanodine, 158
Oxythane, 15

P

Paracide, 49
Paradichlorobenzene, 49; 174
Paraffinic oils, 141
Paraffins, 154
Para-oxon, 137; 172
Parathion, 138; 174
Parathion, S-ethyl isomer, 138
Parathion, S-phenyl isomer, 138
Paris Green, 139
Paris green homologues: butyric, formic, propionic, succinic, valeric, 139
Parpanit, 130
Parrot Green, 139
PCBS, 34
PCI, 34
PCP, 140
PCPBS, 34
PDB, 49
Peanut oil, 157
Peanut oil green (Paris green homologue), 139
Peat, 170
Pellitorine, 107; 171
Pellitorine, cis-trans isomer, 171
Pellitorine, trans-trans isomer, 171
Penchlorol, 140
Penicillin G Potassium, 6
Penicillin G Sodium, 6
Penphene, 183
Penphos, 138
"Penta", 140
Pentabromophenol, 140; 174
Pentacalcium arsenate, 7
Pentachlorophenol, 140; 174
Pentachlorophenol, alkyl homologues, 140
Pentachlorophenoxy acetic acid, 140
2-Pentachlorophenoxy ethanol, 140
2-Pentachlorophenoxyethyl acetate, 140
1-Pentachlorophenoxy-2,3-propane diacetate, 140
1-(Pentachlorophenoxy)-2,3-propanediol, 140
Pentachlorophenyl alkyl ethers: primary Amyl, n-Butyl, n-Dodecyl, n-Hexyl, Methyl, Propyl, 140
α,α,α-2,4-Pentachlorotoluene, 17
α,α,α-3,4-Pentachlorotoluene, 17
d-2-cis-(Penta-2',4'-dienyl)-3-methyl-cyclopent-2-en-ol-1-one, 154
d-cis-Penta-2,4-dienylrethrolone, 154
Pentadimethylamide triphosphoric acid, 132
Pentobarbital, 3
4-(3-Pentyl)-pyridine, 104
Perawin, 177
Perchlormethyl mercaptan, 101
Perchloroethylene, 177
Perchloromethane, 29
Periodic acid, 158
Perm-A-Chlor, 186
Permasan 60, 140
Perthane®, 50
Pestox III, 132
Pestox XV, 20
Petroleum ether, 154
Petroleum oils, 141
Petroleum-β-sulfonates, 141
Petzinol, 186
Phaseolus (plant genus), 132
Phenanthrene, 141
Phenazine, 142
Phenols, 141
Phenothiazine, 142
Phenothiazine, sulfoxide, 142
Phenothiazone, 142
Phenothioxin, 126; 142
Phenoxazine, 142
Phenoxur, 142
Phenthiazine, 142
Phenyl acetyl indanedione, 110; 148
p-Phenylazoaniline, 10
Phenylazo-m-cresol, 10
Phenylazo-o-cresol, 10
p-Phenylazo-dimethylaniline, 10
p-Phenylazo-diphenylamine, 10
1-Phenylazo-2-naphthylamine, 10
p-Phenylazophenol, 10
Phenyl benzoate, 38
l-Phenylbenzothiazole, 154
l-Phenylbenzylthiazole, 142
Phenyl butyl ketone, 104
Phenyl-1-n-butyl-N-methylamine, 131
Phenyl-chlorophenyl-trichloromethane, 17
N-Phenyldiazopiperidine, 126
Phenyl diethyl phosphate, 100; 126
Phenyl diethyl thionphosphate, 100
Phenylephrine, 159
Phenyl ether, 142
Phenylethyl chrysanthemic acid ester, 3
4-Phenyl-2-hydroxythiazole, 106; 135
2-Phenyl-1,3-indanedione, 110
Phenylmercuric chloride, 174
1-Phenyl-3-methyl-5-pyrazole, 143
1-Phenyl-3-methylpyrazolyl-(5)-dimethyl-carbamate, 143
1-Phenyl-3-methylpyrazolyl-(5)-dimethyl carbamate analogues (double substitution replacing phenyl group and the 3-methyl on the pyrazolyl moiety), 143
1-Phenyl-3-methylpyrazolyl-(5)-dimethylcarbamate analogues (substituents replacing the dimethyl of the carbamate moiety), 143
1-Phenyl-3-methylpyrazolyl-(5)-dimethyl carbamate analogues (substituents replacing the 3-methyl-group on the pyrazolyl moiety), 143
1-Phenyl-3-methylpyrazolyl-(5)-dimethylcarbamate analogues (substituents replacing the phenyl moiety), 143
β-Phenylpropionitrile, 1
β-Phenyl propionyl indanedione, 110
α-Phenylpyrrolidine, 130
d-α-Phenyl pyrrolidine, 130
dl-α-Phenyl pyrrolidine, 130
l-α-Phenyl pyrrolidine, 130
α-Phenyl pyrroline, 130
Phenylstyryl ketone, 126
Phenyl sulfide, 142
Phenyl sulfone, 80
Phenyl thiocyanate, 135
Phenyl thiocyanoacetate, 135
1-Phenyl-2-trichloroethanol-1, 17
Phenyl urethane, 6
Phos-Kil, 138
Phosphagen, 158
Phosphates, (diethyl aryl). See Diethyl aryl phosphates
Phosphine oxides: Tri-(p-chlorophenyl), Tri-(ethyl benzene phosphono), 134
Phosphite esters: Dibutyl, Diethyl, Tributyl, Triethyl, 134
Phosphonate esters: Dibutyl 2-methyl-2-propene, Dibutyl 2-propene, Dibutyl B-styrene, Dibutyl trichloromethane, Di-(p-chlorophenyl-ethane), Diethyl p-chlorobenzene, Diethyl 3,4-dichlorobenzene, Diethyl trichloromethane, Triethyl phosphonoacetate, 134
Phosphonates (compound group), 134
Phosphonothioates (compound group), 134
Phosphoramide N-oxide (a biologically functional group), 132
Phosphorodi-(isopropylamidic) fluoride, 20
Phosphorodithioates (compound group), 134
Phosphorothioates (compound group), 134
Phosphorothionates (compound group), 134
Phosphorus, 144
Phthalic acid, methyl-n-hexyl ester, 134
Phthalimide, N-sec.-butyl, 155
Phthalonitrile, 1; 21
Phytotoxicity, 145
α-Picoline, 131
Picolines, 141
Picrotoxin, 93
Pinacolone, 148
Pinene, 104; 166
Pinene, ethylene glycol ether, 146
Pinoresinol, 160; 171
Pinoresinol dimethyl ether, 160
Pinosylvin, 174
Piperic acid, 146
Piperidine, 131
Piperine, 103; 146; 171
Piperonal, 171
Piperonyl alcohol, 171
Piperonyl butoxide, 146; 171
Piperonyl chrysanthemic acid ester, 3
Piperonyl cyclohexenone, 147; 174
Piperonyl cyclonene, 147; 171
Piperonylic acid, 171
Piperonylidene malonic acid, diethyl ester, 134
Pitch, 141
Pitch greases, 141
Pival®, 148
Pivalyl indan(e)dione, 148

Note: The numbers following the entries indicate the Section in which the entry occurs.

2-Pivalyl-1,3-indan(e)dione, 148; 171
Pivalyl indanedione, Fe^{++} salt, 110
2-Pivalyl-1-indanedione Sodium, 6
Pivalyl valone, 148
Plants, insecticidal: families and genera of plants of known or reputed insecticidal significance, 149
Podophyllotoxin, 6
Polyacrylon rubber, 170
Polyethylene polysulfides, 126
Polymethylenes, 141
Polymixin, 6
Potasan®, 62
Potassium fluoaluminate, 42
Potassium fluoride, 94
Potassium fluosilicate, 42
Potassium selenate, 172
Potassium selenite, 172
Potassium silicofluoride, 42
Potassium thiocyanate, 135
Powdered milk, 170
Precipitated Sulfur, 168
Precipité Blanc, 118
Primula (plant genus), 132
Prolan®, 174
Propanol, 104
Propenene nitrile, 1
Propene oxide, 151
Propionic acid, diester with 1,5-pentanediol, 155
Propionitrile, 1
Propionyl chloride, 104
Propionyl indanedione, 110
2-Propionyl-1,3-indandione, 148
N-Propylacetamide, 91
N-Propylacetanilide, 91
n-Propyl acetate, 104
n-Propylamine, 104
Propyl bromide, 104
n-Propyl bromide, 104
Propyl butyrate, 104
n-Propyl chlorocarbonate, 104
O-Propyl-O-p-chlorophenyl methane phosphonate, 134
O-Propyl-O-2,4-dinitro-phenylmethane phosphonate, 134
Propylene chlorhydrin, 104
Propylene chloride, 150
Propylene dichloride, 150
α,β-Propylene dichloride, 150
Propylene oxide, 151
n-Propyl formate, 104
n-Propyl iodide, 82
n-Propyl isome, 152; 171
n-Propyl isome derivatives: C_2H_5, n-C_3H_7, n-C_4H_9, $C_6H_5CH_2$, C_6H_{11}, CH_2CH_2Cl, CH_2CH_2SCN,  $CH_2\underbrace{CHCH_2CH_2CH_2}_{O}$, 154
n-Propyl mercaptan, 104
2-n-Propyl-4-methylprimidyl-(6)-dimethylcarbamate, 153; 172
Propyl pentachlorophenyl ether, 140
6-(Propylpiperonyl)-butylcarbityl ether, 146
Propyl propionate, 104
n-Propyl-n-propionate, 104
2-n-Propyl-pyridine, 104
4-n-Propyl-pyridine, 104
Protoveratridine, 159
Protoveratrine A, 159
Protoveratrine B, 159
Protoverine, 159
Prussic acid, 101
Pseudo-cumene, 104
Pseudo-jervine, 159
Pyramat, 153; 172
Pyrazine dimethyl carbamate, 153
Pyrazolone, 63
Pyrazothion, 64
Pyrazoxon, 63; 172
Pyrenone® Wheat Protectant, 146
Pyrethric acid, 154
Pyrethrins I,II, 154
Pyrethroids, various synthetic, 154
Pyrethrolone, 154
Pyrethrolone esters of mono- and di- chrysanthemumcarboxylic acids, 154
Pyrethrolone esters of various acids: Acetic, Benzoic, Camphor, Cinnamic, Citronellic, Crotonic, Dichloroacrylic, β-Fencholic, Geranium, Isobutyric, Malonic, o-Methoxybenzoic, Piñon, Undecylenic, 154
Pyrethrolone, pulegenic acid ester, 154
Pyrethrum, 154
Pyrethrum C^{14} - labelled, 154
Pyrexcel®, 133
Pyridazine dimethyl carbamate, 153
Pyridine, 6; 131
Pyridine dimethyl carbamate, 153
Pyridines, 141
Pyridyl-N-benzylchloride, 131
3-Pyridyl-1-n-butyl-N-methylamine, 131
3-Pyridyl-2-ethyl-N-ethylamine, 131
Pyridylmercuric chloride, 174
Pyridylmercuric stearate, 174
Pyridyl-N-methylpyrrolidine, 130
β-Pyridyl-α-N-methylpyrrolidine, 130
l-2-(3'-Pyridyl)-piperidine, 5
2-(3'-Pyridyl)-pyrrolidine, 131
Pyrimidine dimethyl carbamate, 153
Pyrocatechol, 154
Pyrogallol, 154
Pyrolan, 143; 172
Pyrophosphates (compound group), 134
Pyrophosphoramidates (compound group), 134
Pyrophosphoramides (compound group), 134
Pyrophosphoric tetrakis dimethylamide, 100; 126
Pyrophosphoryl tetrakis dimethylamide, 132
Pyrrole, 131
Pyrrolidine, 131
l-3-(2'-Pyrrolidyl)-pyridine, 131
Pyruvic acid, 164

Q

Q 137 Experimental Insecticide, 50
Quinaldine dimethyl carbamate, 153
Quinoline, 104; 131
Quinoline dimethyl carbamate, 153

R

R-242
Repellents, 155
Resinous bodies, 141
Resistance, 156
Rhothane®, 16
Rosa (plant genus), 132
"Rotenoids", 157
Rotenol, 157
Rotenolone, 157
Rotenone, 157
Rotenone-Bentonite, 157
Rotenone hydrochloride, 157
Rotenone-lampblack, 157
Rotenonone, 157
Rubijervine, 159
Rutgers 612, 91
Ryanex®, 158
Ryania, 158; 174
Ryanodine, 158; 174

S

Sabadilla, 159
Sabadilla officinarum, 159
Sabadillic acid, 159
Sabadilline, 159
Sabadine, 159
Sabadinine, 159
Sabatine, 159
Safranin (bluish), 39
Salicyl aldehyde, 101
Salufer, 165
Sand, 170
Santobrite, 140
Santomerse D, 140
Santophen 20, 140
Saran rubber, 170
Scabrin, 107; 171
Schoenocaulon officinale, 159
Schradan, 132; 172
Schweinfurth Green, 139
Scorodite, 7
Selenium, compounds of, 179
Selenolphosphoric acid esters, 172
Senecioyl indanedione, 110
Sesame oil, 154; 160
Sesamin, 160; 171
Sesamolin, 160
Sesquiterpene-containing oils, 157
Silver, 170
Sinox, 76
666 (Six-six-six), 114
SNP, 138
Sodium aluminofluoride, 42
Sodium aluminum fluoride, 42
Sodium arsenate, 161
Sodium arsenite, 162
Sodium azide, 132
Sodium biborate, 21
Sodium p-chlorobenzene sulfonate, 17
Sodium chlorophenate, 140
Sodium dinitro-o-cresylate, 76
Sodium 4,6-dinitro-o-cresylate, 76
Sodium fluoacetate, 164; 172
Sodium fluoaluminate, 42
Sodium fluoride, 163
Sodium fluoroacetate, 164; 172
Sodium fluosilicate, 165
Sodium meta-arsenate, 161
"Sodium meta-arsenite", 162
Sodium methyl thiouracil, 76
Sodium monofluoroacetate, 164
Sodium oleyl sulfate, 157
Sodium paranitrophenate, 137
Sodium pentachlorophenate, 140; 174
Sodium pyroborate, 21
Sodium selenate, 166; 172
Sodium selenite, 172
Sodium silicofluoride, 165
Sodium tetraborate, 21
Sodium thiocyanate, 135
Soilfume, 87
Δ^5 - Solanidene-3(β), 12-α-diol, 159
Sonneborn oil #51, 167
Soybean oil, 157
Soybean oil green (Paris green homologue), 139
Spilanthol, 107; 171
Spindle oils, 141
Sponge rubber, 170
Stainless steel, 170
Stearic acid salts, 141
Stearyl thiocyanate, see n-Octadecyl thiocyanate
Stilbene, 126; 174
Stoddard solvent, 141
Stove oils, 141
"Straight-run" gasolenes (gasolines), 141
Streptomycin SO$_4$, 6
Strobane®, 167
Strontium fluoride, 94
Styryl cyanide, 1
Sublimed sulfur, 168
Succinamic acid, N, N'-dipropylethyl ester, 155
Sudan III, 154
Suede, 170
Sulfanilamide, 6
Sulfatep, 178
Sulfenone® (Sulfenone), 36
Sulfobenzide, 80
Sulfonated fatty acids, 141
Sulfonated Lorol®, 173
Sulfone, 171
Sulfotepp, 178
Sulfox-Cide (now: Sulfoxide®), 133
Sulfoxide®, 133; 171
Sulfur, 168
Sulfur dioxide, 169
Sulfurous anhydride, 169
Sulfurous oxide, 169
Sulfuryl fluoride, 170
Sulphenone, 36
Sulphur, 168
Sumatrol, 46, 157
Summer oils, 141
Synergism, 171
Synergists, 171
Synkayvite (Roche), 148
Synthetic 3956 (Hercules Powder Company), 183
Systemic insecticides, 172
Systox®, 59; 172

T

"Tabun", 134

Note: The numbers following the entries indicate the Section in which the entry occurs.

Tar acids, 141
Tar camphor, 129
Tar distillates, 141
Tar oils, 141
Tars (coke-oven), 141
Tartaric acid, diisopropyl ester, 155
TDE, 16
Tea seed oil, 157
Tectoquinone, 174
Tedion V 18, 175
Temperature and insecticidal action, 173
"Ten Eighty", 164
TEP, 179
Tephrosin, 46; 157
TEPP, 172; 179
Termites, (repellents and insecticides for), 174
Terpene polychlorinates, 167
Terpineol, 154, 173
Terpinyl thiocyanoacetate, 106; 135
Terramycin HCl, 6
Tetraalkyl aryl triphosphate esters: sym-Phenyl tetrabutyl, sym-Phenyl tetrapropyl, 134
Tetraalkyl pyrophosphate esters: Tetrabutyl, Tetraethyl, Tetrapropyl, 134
1,1,1,2-Tetrachloro-2,2-bis(p-chlorophenyl)ethane, 17
2,2,3,4-Tetrachlorobutyronitrile, 1
Tetrachlorodiphenylethane, 16
2,4,5,4'-Tetrachlorodiphenyl sulfone, 175
Tetrachloroethane, 176
Tetrachloroethylene, 177
Tetrachloromethane, 29
Tetrachlorophenate, 61
Tetrachlorophenol, 174
2,3,4,6-Tetrachlorophenyl trichlorobenzyl ether, 140
2,2,3,3-Tetrachloro-1,1,4,4-tetrakis (p-chlorophenyl) butane, 17
α,α,α-2-Tetrachlorotoluene, 17
α,α,α-3-Tetrachlorotoluene, 17
α,α,α-4-Tetrachlorotoluene, 17
Tetradecyl thiocyanate, 23
n-Tetradecyl thiocyanate (= Myristyl thiocyanate), 111
Tetraethyl ammonium, 159
Tetraethyl dithionophosphate, 100
Tetraethyl dithionopyrophosphate, 126; 178
Tetraethyl dithiopyrophosphate, 134; 178
Tetraethyl monothionophosphate, 100
Tetraethyl monothionpyprophosphate, 126
Tetraethyl pyrophosphate, 126; 172; 179
Tetraethyl thiuram disulfide, 126
Tetrahydrochlorophenyl ether, 140
Tetrahydrofurfuryl thiocyanoacetate, 106; 135
1,2,5,6-Tetrahydro-o-methyl benzoic acid, 14
1,2,5,6-Tetrahydro-o-methylbenzyl ester, 14
Tetrahydronaphthalene, 104
Tetrahydropyrethrin I, 154
Tetraisopropyl pyrophosphate, 179
1,1,2,2-Tetrakis (p-chlorophenyl) ethylene, 17
Tetrakis dimethylamino phosphonous anhydride, 132
Tetralex, 177
4-α,α,β - Tetramethyl-n-butylphenyl thiocyanoacetate, 106; 135
Tetramethyl dithiopyrophosphate, 134
Tetramethylene thiocyanate, 135
Tetramethylene thiocyanohydrin, 135
3,5,7,9-Tetramethylphenothiazine, 142
Tetramethyl pyrophosphate, 179
Tetramethyl thiuram disulfide, 126
Tetramethyl thiuram monosulfide, 126
2,2',4,4'-Tetranitrodiphenyl, 126
Tetranitrophenothiazine sulfoxide, 142
Tetra-n-propyl dithionopyrophosphate, 180
Tetrapropyl dithiopyrophosphate, 180
Tetra-n-propyl dithiopyrophosphate, 180
Tetrasodium salt of 2-methyl-4,4-naphthohydroquinone diphosphoric acid, 148
Tetron, 179
Thallium (element), 181
Thallium acetate, 181
Thallium carbonate, 181
Thallium fluoride, 181
Thallium nitrate, 181
Thallium sulfate, 181
Thallous sulfate, 181
Thanite®, 106; 135
2-Thenyl benzoate, 38
2-Thenyl salicylate, 38
Theophylline, 138
Thialdine, 126
Thianthrene, 142
α-Thienyl-α-pyrrolidine, 130
α-Thienyl-α-pyrroline, 130
Thiocyanates: Benzyl, n-Butyl, Capryl, n-Dodecyl, Ethyl, 2-Ethylhexyl, n-Hexadecyl, n-Hexyl, Isopropyl, Lauryl, Methyl, n-Octadecyl, Phenyl, n-Tetradecyl, 135
Thiocyanates (organic), 135
β-Thiocyanoacetate of diethyleneglycol monobutyl ether, 135
Thiocyanoacetates: 2-Butoxyethyl, 4-tert.-Butylcyclohexyl, 2-Caproxyethyl, Capryl, Carvomenthyl, Cyclohexyl, Decahydro-2-naphthyl, 2-(2-Ethoxyethoxy) ethyl, 2-Ethylhexyl, 2-Fenchoxyethyl, Fenchyl, n-Hexyl, Isobornyl, Lauryl, 2-Methoxyethyl, Methyl, 1-Methyl-3-cyclohexyl-n-propyl, 2-(1-Methyl-3- [α-tetrahydrofuryl])-n-propoxyethyl, 1-Methyl-3-(α-tetrahydrofuryl)-n-propyl, 2-β-Naphthoxyethyl, α-Naphthyl, Phenyl, Terpinyl, Tetrahydrofurfuryl, β,β'-Di-(α-tetrahydrofuryl)-diethylcarbinyl, 4-(α,α,β,γ-Tetramethyl-n-butyl)-phenyl, Thiocyano-4-cyclohexyl butanone-(2), 135
Thiocyanoacetone, 106
ω-Thiocyanoacetophenone, 135
p-Thiocyanoaniline, 23; 135
2- Thiocyano-4-tert.-butylcyclohexanone, 106; 135
2-Thiocyanocyclohexanone, 106; 135
Thiocyano-4-cyclohexylbutanone-2, 106
5-Thiocyano-2,3-dihydropyran, 106; 135
2-Thiocyanoethyl esters of C_{10} - C_{18} aliphatic acids, 182
β-Thiocyanoethyl ethyl ether, 135
β-Thiocyanoethyl laurate, 182
β-Thiocyanoethyl methyl ether, 135
β-Thiocyanoethyl phenyl ether, 135
Thiocyanogen compounds, 135
1-Thiocyanoheptene-(1), 106; 135
Thiocyanohydrin, 135
α-Thiocyanoketones, 135
ω-Thiocyano-4-methoxyacetophenone, 135
Thiocyanomethyl phenyl ketone, 135
2-Thiocyanooctane, 135
γ-Thiocyanopropyl phenyl ether, 135
Thiocyanotetrahydroionone, 106; 135
Thiodiphenylamine, 111; 142
Thiokol rubber, 170
Thiol-alcohols, 172
Thionol, 142
Thionophosphates (compound group), 134
Thionyl chloride, 104
Thiophenol, 101; 126
Thiophos, 138
Thiophosphoric acid, 137
Thiophosphoric acid esters, 172
Thiourea, 6; 21
Timbo, 115
Tin, tetra-alkyl and tetra-aryl compounds of, 187
TM 12008, 60; 172
TM 12009, 65; 172
TM 12013, 66; 172
α-Tocopherol, 166
TOCP, 20; 134
Toluene, 104; 141
1-(o-Tolylazo)-2-naphthylamine, 10
p-Tolyl benzoate, 91
d-2-p-Tolylpyrrolidine, 131
l-2-p-Tolylpyrrolidine, 131
d-α-p-Tolylpyrrolidine acid *d*-tartrate, 130
l-α-p-Tolylpyrrolidine acid *l*-tartrate, 130
Toxakil, 183
Toxaphene®, 174; 183
Toxaphene®, arsonated, 183
Toxicarol, 46
l - α-Toxicarol, 157
Trethylene, 186
Tri, 186
Trial, 186
Trialkyl and Triaryl acid phosphate esters: Triallyl, Tri-(β-chloroethyl), Tri-(o-chlorophenyl), Tricresyl, Triethyl, Tri-(2-ethylhexyl), Trimethallyl, Trimethyl, Triphenyl, Tri-(2,4,6-trichlorophenyl), 134
1-Tribromo-2,2-bis-(p-bromophenyl) ethane, 17
1-Tribromo-2,2-bis-(p-chlorophenyl) ethane, 17
Tri-calcium arsenate, 25
Trichloroacetic acid, 186
Trichloroacetonitrile, 184
1,2,3-Trichlorobenzene, 13
1,2,4-Trichlorobenzene, 13
1,3,5-Trichlorobenzene, 13
2,4,6-Trichlorobenzyl ether, 140
2,4,6-Trichlorobenzyl 2,4,5-trichlorophenyl ether, 140
1-Trichloro-2,2-bis-(p-acetoxyphenyl) ethane, 17
1-Trichloro-2,2-bis-(p-bromophenyl) ethane, 17
1-Trichloro-2,2-bis-(p-tert.-butylphenyl) ethane, 17
1 -Trichloro-2,2-bis-(4-chloro-3,5-dinitrophenyl) ethane, 17
1-Trichloro-2,2-bis-(5-chloro-2-hydroxyphenyl) ethane, 17
1-Trichloro-2,2-bis-(5-chloro-2-methoxyphenyl) ethane, 17
Trichloro-bis-(4-chlorophenyl)-ethane, 17
1,1,1-Trichloro-2,2-bis-(p-chlorophenyl)-ethane, 17
1-Trichloro-2,2-bis-(3,5-dichloro-2-hydroxyphenyl) ethane, 17
1-Trichloro-2,2-bis-(3,5-dichloro-2-methoxyphenyl) ethane, 17
1-Trichloro-2,2-bis-(3,5-dichloro-4-methoxyphenyl) ethane, 17
1-Trichloro-2,2-bis-)2,5-dimethoxyphenyl) ethane, 17
1-Trichloro-2,2-bis-(3,4-dimethoxyphenyl) ethane, 17
1-Trichloro-2,2-bis-(p-fluorophenyl) ethane, 17
1,1,1-Trichloro-2,2-bis-(p-fluorophenyl) ethane, 19
1-Trichloro-2,2-bis-(p-hydroxyphenyl) ethane, 17
1-Trichloro-2,2-bis-(p-methoxyphenyl) ethane, 17
1,1,1-Trichloro-2,2-bis-(p-methoxyphenyl) ethane, 120
2,2,3-Trichlorobutyronitrile, 1
2,2,4-Trichlorobutyronitrile, 1
1-Trichloro-2-(p-chlorophenyl)-2-(m-chlorophenyl) ethane, 17
1-Trichloro-2-(p-chlorophenyl)-2-(o-chlorophenyl) ethane, 17
2-Trichloro-1-p-chlorophenylethanol, 17
1-Trichloro-2,2-dichloro-3,3-dichloro-4,4-bis-(p-chlorophenyl) butane, 17
1-Trichloro-2,2-diphenyl ethane, 17
1-Trichloro-2,2-di-p-tolylethane, 17
Trichloroethane, 185
1,1,1-Trichloroethane, 185
1,1,2-Trichloroethane, 185
2,2,2-Trichloroethyl-*dl*-trans-chrysanthemate, 154
Trichloroethylene, 186
Trichloronitromethane, 37
1-Trichloro-2-(p-nitrophenyl)-2-(m-nitrophenyl) ethane, 17
1-Trichloro-2-phenyl-2-biphenyl ethane, 17
1-Trichloro-2-phenyl-2-(p-chlorophenyl) ethane, 17
Tri-(p-chlorophenyl) thionphosphate, 100; 126
1,2,3-Trichloropropane, 45
2,2,3-Trichloropropionitrile, 1
α-Trichlorotoluene, 17
Triclene, 186
Tri-Clene, 186
Tri-o-cresyl phosphate, 20; 134
Trielene, 186
Trielin, 186
Triethyl phosphate, 100; 126; 134
Triethyl thiophosphate, 134
Triethyl tin acetate, 187
Triethyl tin acrylate, 187
Triethyl tin benzoate, 187
Triethyl tin bis-(chlorophenyl) acetate, 187
Triethyl tin *d*-trans-chrysanthemumate, 187
Triethyl tin formate, 187
Triethyl tin hydroxide and its esters; insecticidal activity, 187
Trilene, 186
Triline, 186
Trimagnesium orthoarsenate, 116
Tri-(p-nitrophenyl) thionophosphate, 100; 126
Tri-orthocresyl phosphate, 20
Triphenyl phosphate, 100; 126; 174
Triphenyl phosphine, 100; 126
Triphenyl phosphite, 174
Triphenyl stibine, 174
Triphenyl thionphosphate, 100; 126
Triphosphoric acid pentadimethyl amide, 132
Tripterygium wilfordii, 188

Note: The numbers following the entries indicate the Section in which the entry occurs.

Tris-(dimethylamido) monoethyl pyrophosphate, 172
Tri-o-tolyl phosphate, 100; 126
Tritox (I.G. Farbenindustrie), 184
Tuba, 157
Tubaic acid, 157
Tubatoxin, 157
Tung oil, 157
Turpentine, 104

U

Ultrasene, 167
2-(6-Undecyl)-pyridine, 104
Undecyl thiocyanate (secondary), 111
Unrefined aliphatic oils, 141
Urethane, 6

V

Valeric aldehyde, 104
Valone®, 110; 171
Van Dyk 264, 92
Vanillin, chrysanthemic acid ester of, 3
Vanilloyl zygadenine, 159
Vapophos, 138
Vapotone, 179
Velsicol 104, 96
Velsicol 1068, 30
Velsicols, 141
Veracevine, 159
Veralba, 159
Veratramine, 159
Veratric acid, 159
Veratridine, 159
Veratrimine, 159
Veratrine, 3; 159
Veratrine hydrochlorides, 159
Veratrone, 159
Veratrosine, 159
Veratroyl zygadenine, 159
Veratrum viride, 159
Veriloid, 159
Vestrol, 186
Vienna Green, 139
Vikane (Dow Chemical Company), 170
Vinegar naphtha, 84
Vinyl cyanide, 1
Vinyl trichloride, 185
Vitamin K, 110; 148
Vitamin K, synthetic, 148
Vitran, 186

W

Wakefield half-white oil, 173
Westrosol, 186
Wheat gluten, 170
White arsenic, 8
White gasoline, 141
White oil, 154
White spirit, 154
White wheat flour, 170
Wilfordine, 188
Wilforgine, 188
Wilforine, 188
Wilfortrine, 188
Wilforzine, 188
Wool, 170

X

Xanthone, 126; 174
Xanthone manufacture by-products, 174
Xylene, 104; 141
Xylenol, 157
Xylenols, 141

Y

Yellow phosphorus, 114

Z

Zinc, 170
Zinc arsenate, 7
Zinc arsenite, 7
Zinc dimethyl dithiocarbamate, 174
Zinc lake (acetic acid) B-chloroanthroquinone, 174
Zinc lake (acetic acid) chrysazin, 174
Zinc lake (acetic acid) quinizarin, 174
Zinc phosphide, 11
Zinc sulfate, 7
Zygadenine, 159
Zygadenine monoesters: Veratroyl, Vanilloyl, 159

Note: The numbers following the entries indicate the Section in which the entry occurs.